JANUARY, 1929 NUMBER 1

ANNALS OF INTERNAL MEDICINE

PUBLISHED BY

The American College of Physicians

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Issued Monthly

Ann Arbor, Michigan

ANNALS OF INTERNAL MEDICINE

OFFICIAL PERIODICAL OF THE AMERICAN COLLEGE OF PHYSICIANS

DEPARTMENT OF REVIEWS

The Journal will make an especial feature of the review of monographs and books bearing upon the field of Internal Medicine. Authors and publishers wishing to subject such material to the purposes of review should send it to the editor. While obviously impossible to make individual reviews of all material, an acknowledgment of all matter sent will be made in the department of reviews.

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Price for volume, net, postpaid, $7.00, United States, Canada, Mexico, Cuba, $7.50 other countries

Entered as second class matter at the Post Office, Ann Arbor, Michigan

The Hemopoietic Effect of Nuclear Extractives in Human Anemias*

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WITH no more than passing reference (1, 2, 3, 4) to the experimental work upon which the following clinical studies have been founded, we wish in this paper to relate briefly observations we have made on the effect of nuclear extractives in the treatment of anemia in human patients. The nuclear extractives used, as reported elsewhere, have been obtained by the methods of Hammarsten and of Kossel-Neumann from various organ sources, and have been considered to be nucleo-proteins and the sodium salts of nucleic acids. An unknown hemopoietic stimulant exists in both of these nuclear extractives, and because from both experimental and clinical suggestive evidence we have thought a greater effect upon blood regeneration was seen from the use of both extractives in combination than from the use of either one alone, we have administered to anemic patients capsules containing one-fourth gram of each extractive. In the earlier part of the clinical work we employed the intravenous injection of from one-fourth to one gram of the sodium salts of nucleic acids obtained from the washed nuclei of the blood cells of the fowl. There was observed, however, in about one-half of the patients so treated, a serum-like reaction of sufficient degree to make this method objectionable. In consequence, oral administration of the extractives was adopted with seemingly the same effect upon the blood picture.

In the entire study thus far made we have obtained nuclear extractives from eight different organs; and the percentages of extractives obtained per given weight of organ substance has been as follows: chicken corpuscles about 3 per cent, beef spleen 2.4 per cent, beef liver 1.8 per cent, beef kidney 0.9 per cent, beef heart muscle 0.5 per cent, salmon liver 2.4 per cent, beef thymus per cent and beef pancreas per cent not determined. All of the above extractives, with the exception of those obtained from beef heart muscle, have been used in the produced anemia of experimental animals. The animals have shown the same type of response in reticulated cells, hemoglobin content and in red blood cell counts that has been seen in anemic animals and in human patients with pernicious anemia to whom a high

*Aided by grant No. 128 from the Committee on Medical Research of the American Medical Association.

liver diet has been administered. The hemopoietic stimulation observed, however, has seemingly shown a more definite relation to the quantity of extractives administered than to the organ from which they were obtained. The best results followed the administration of extractives from chicken corpuscles and the next most marked results from the use of extractives from beef spleen and from salmon liver. Both of the latter extractives gave better responses than did those from beef liver. For an as yet unknown reason the extractives from thymus have given the least response of all. In the anemias of human patients we have employed thus far the extractives obtained from chicken blood cells, beef liver and beef spleen, and we have seen in these patients, for the most part, similar effects upon the blood production.

Nuclear Extractives Obtained from the Washed Nuclei of Chicken Blood Cells

It was found experimentally that the hemopoietic stimulant existed only in the nucleus of the chicken blood cell. The cytoplasm of the cell alone —and consequently the hemoglobin element of the cell—possessed no power to stimulate blood formation in the animal body. It was from the washed nuclei of the blood cells, therefore, that we obtained the first nuclear extractives used in this series of studies.

Tables I and II, respectively, give, briefly, the important data in a series of pernicious anemia patients and in a series of patients having secondary anemias. A temporary slight rise in hemoglobin and in the red cell count was observed in most of them.

Patient No. 1, table I, suffered a severe reaction from the intravenous administration of the extractives, and his blood counts showed no temporary rise in hemoglobin and red cells, as the blood of the other two patients did show. This patient had had a splenectomy done some months before. We have seen the same response from the intravenous injection of similar nuclear extractives in splenectomized rabbits. The third patient showed no more effect from the long continued use of liver than she had temporarily shown in response to the injection of 0.5 gm. sodium nucleate.

In a similar way the patients having chronic secondary anemias showed usually a temporary rise in hemoglobin and red cell content in response to one administration of sodium nucleate. In patient No. 2, bleeding uterine fibroids seemingly prevented any rise, and there was also no effect upon the blood seen from the use of liver. In patient No. 5 a temporary rise in blood count was seen to follow each of two injections of 0.25 gm. doses.

The effect of the oral administration of nuclear extractives obtained from whole chicken blood and the effect of the oral administration of the washed nuclei themselves is now being studied and a report of these observations will be made later.

Nuclear Extractives Obtained from Beef Liver

A larger number of patients with anemia have been treated clinically by us with the nuclear extractives ob-

SODIUM NUCLEATE FROM WASHED NUCLEI OF CHICKEN BLOOD CELLS
CASES OF PRIMARY ANEMIA

TABLE I

No.	Date	Name	Age	Sex	Diagnosis	Hb. %	RBC	Retic. %	V.I.	Therapy	Duration of Anemia Remarks
1	10-27-26	AEWP	68	M	Pernicious	58	2.23		1.45	1 gm.	2-3 years
	10-29-26				Anemia	49	1.95			Intravenously	Severe reaction lasting three days
	11-16-26					57	2.25				
	1-13-27					40	1.61				Patient continued on liver diet without change in blood picture until his death 4-20-27. Had previously had a splenectomy and a cholecystectomy
2	11- 5-26	MHC	73	F	Pernicious	72	2.85		1.29	0.5 gm.	1 year
	12- 1-26				Anemia	87	3.67			Intravenously	Chill and fever
3	11- 3-26	AE	62	F	Pernicious	86	3.82		1.15	0.5 gm.	3 years
	11-19-26				Anemia	96	4.22		1.14	Intravenously	Chill and fever Continued on liver diet until death on 9-8-27

SODIUM NUCLEATE FROM WASHED NUCLEI OF CHICKEN BLOOD CELLS
CASES OF SECONDARY ANEMIA
TABLE II

No.	Date	Name	Age	Sex	Diagnosis	Hb. %	RBC	Retic. %	V.I.	Therapy	Duration of Anemia Remarks
1	11- 6-26 12- 3-26 12-30-26	BT	39	F	Chr. Cholecystitis	69 80 65	4.41 4.67 4.39			0.5 gm. Intravenously	3 years No reaction
2	11-23-26 11-29-26	CBW	39	F	Bleeding Uterine Fibroids	64 57	4.21 4.48			0.75 gm. Intravenously	3 years Chill, fever, vomiting Liver feeding also gave no effect
3	12-31-26 1- 5-27	MM	32	F	Chr. Cholecystitis	85 94	4.36 4.44			0.5 gm. Intravenously	4½ years No reactions
4	12-21-26 12-21-26 12-22-26 1- 5-27	RGL	54	F	Chr. Cholecystitis	36 38 35 27	2.03 2.12 2.01 1.34		1.05	0.5 gm. Intravenously	6 months Chill, fever, headache Liver feeding also gave no effect. Death
5	10-18-26 10-29-26 11-10-26 12-16-26 12-29-26	JP	62	F	Chr. Cholecystitis	81 78 73 78 75	3.35 4.17 3.28 3.82 3.25			0.25 gm. Intravenously 0.25 gm. Intravenously	6 months No reaction Chill for ½ hr.
6	1-20-27 1-28-27 2- 7-27	BM	70	F	Chr. Cholecystitis	81 89 83	4.29 4.42 3.21			0.5 gm. Intravenously	4-5 years No reaction
7	11- 8-26 3-17-27	HHN	40	F	Chr. Cholecystitis	79 88	4.80 4.85			0.25 gm. Intravenously	3 years No reaction Cholecystectomy 6-21-26

tained from other sources than chicken blood cells, and especially from beef liver, because of the greater ease of manufacturing them in quantity and also because of the present interest in the liver treatment of pernicious anemia. (See tables III and IV, and graphs 1, 2, and 3). We have been able in several instances to run like cases as rough clinical controls. We have also on several occasions treated a given patient with nuclear extractives from liver, from spleen and by liver feeding for stated periods of time to compare if possible the relative stimulant effect of the different substances. In the main, both in the case of primary anemia and in that of secondary anemia like effects have been noted. Our study of pernicious anemia patients during the past year has shown a variation in individual response seemingly due to the fact that a number of the patients had been eating liver before coming to us. In these patients the rise in the reticulated cells has been modified or absent. Case 6, table III, illustrates this point well. Case 7 indicates the necessity of using sufficiently large doses of the extractives.

Patients with secondary anemias showed a less uniform response to the administration of nuclear extractives, and to liver feeding, than did patients suffering from pernicious anemia. However, those patients who had suffered an acute anemia from hemorrhage, from an acute and transitory infection, or even in certain instances in which the cause has not been recognized, have shown quite as dramatic a response to treatment as any person with pernicious anemia. Compare, for example, in table IV, cases Nos. 5, 6, 7, 8, 9, 10, 11, 12, 14, 15 and 16. Rough clinical controls have been run as of cases Nos. 10-A, 13-A, 14-A, 15-A, and 16-A. The identical twins, Nos. 13 and 13-A were under observation and control very unsatisfactorily but an obvious improvement was noted in the treated patient over the progress of the untreated one. The anemia of chronic cholecystitis did not seemingly respond much until after the gallbladder was removed. Then, however, the patient treated with nuclear extractives, or with liver feeding, seemingly regained a normal blood content and a clinical recovery more rapidly than the patient not so treated. The same statement may be made in regard to patients with anemia due to uterine fibroids, hyperplastic sinusitis, etc. This point is stressed because there is now a widespread suspicion that the use of liver or its extractives holds a certain specificity for pernicious anemia and that persons suffering from secondary anemias are unimproved by their use. This suspicion is wholly at variance with our experience. Surely, case No. 6 belies this assumption, for the child had been treated for months with dietetic and medicinal measures without effect and the use of 3 gm. daily of nuclear extractives for a period of seven weeks produced quite as noteworthy a response in blood content and clinical recovery as could be seen in pernicious anemia. We have been of the opinion that the probable cause of failure to gain on the part of some persons with secondary anemia lies in the relative balance be-

SODIUM NUCLEATE AND NUCLEOPROTEIN FROM LIVER
CASES OF PRIMARY ANEMIA

TABLE III

No.	Date	Name	Age	Sex	Diagnosis	Hb. %	RBC	Retic. %	V.I.	Therapy	Duration of Anemia Remarks
1	11-28-27	JE	80	M	Pernicious	35	1.15			450 cc. whole blood	44 years
	12-10-27				Anemia	35	2.26			450 cc. whole blood	Left hospital feeling well
	12-15-27					43	2.26			1 gm. tid increased	
	1- 9-28					72	3.68			to 2 gm. tid in one	
	3-22-28					83	3.79			week	
2	2- 8-28	WL	62	M	Pernicious	41	1.73	1.3	1.23	2 gm. tid	Second relapse of anemia
	2-15-28				Anemia	43	2.08	8.0			Graph No. 1
	2-22-28					73	3.16	24.0			Left hospital feeling well
	2-24-28					104	5.12	2.0			
3	1-29-28	EC		M	Pernicious	38	1.26			1 gm. tid	
	1-26-28				Anemia	43	1.43			2 gm. tid	
	1-30-28					50	2.04			3 gm. tid	
	2-28-28					90	4.36				
	3-26-28					90	4.40				Continues to feel well
4	2- 2-28	OP		M	Pernicious	28	1.03			High protein diet—	
	2-23-28				Anemia	25	0.97			profoundly ill	
	2-27-28					28	1.02			Iron citrate	
	3-12-28					57	2.28			4 gm. tid—started	Marked clinical improve-
	3-26-29					80	3.19			6 gm. tid	ment

TABLE III, Continued

5	4-13-27	KAD	79	F	Pernicious	56	2.14		1.33	2 gm. tid	Acute relapse for 2 wks.
	4-15-27				Anemia	62	2.30				Death—with rising hemo-
	4-18-27					70	2.07				globin
6	3-14-28	ELP	42		Hyperplastic	114	4.50	0.1		Previous	Weakness, dizziness and
	3-21-28				Sinusitis					liver feeding	anemia, since Nov. 1927
	3-30-28				Dental sepsis	93	4.43		1.14	and liver	Radical antrum op.
	4-13-28				Pern. Anemia?	87	4.17	0.3		extracts	Dental extraction
	4-28-28					81	4.21	6.	1.14	Off liver 1 week	Marked clinical improve-
						90	4.10			Off liver 2 weeks	ment
										3 gm. tid	
7	9-10-27	LHS		M	Pernicious	42	1.47			1 gm. tid	Marked clinical improve-
	9-20-27				Anemia	41	1.32			1.5 gm. tid	ment
	10- 1-27				Diabetes	61	1.88				
	10-10-27					66	2.35				
	10-29-27					83	3.25			2 gm. tid	
	11-12-27					90	3.58				
	11-25-27					91	4.17				
	12-20-27					100	3.82				

SODIUM NUCLEATE AND NUCLEOPROTEIN FROM LIVER
CASES OF SECONDARY ANEMIA

TABLE IV

No.	Date	Name	Age	Sex	Diagnosis	Hb. %	RBC	Retic. %	V.I.	Therapy	Duration of Anemia Remarks
1	4- 2-27 4-10-27	JK	69	F	Chr. Chole-cystitis	76 91	4.12 4.66			1 gm. tid	1 year
2	4- 4-27 4-11-27	GC	45	F	Uterine Hemorrhage	84 88	4.65 4.73			1 gm. tid	3½ years
3	3-25-27 4- 7-27	AJL	38	F	Chr. Chole-cystitis	75 84	4.40 4.62			0.5 gm. tid	3 years
4	3-15-27 3-17-27 4- 1-27 4- 9-27	GLS	50	F	Uterine Fibroid	59 61 73 65	3.89 3.98 4.66 4.26			0.5 gm. tid 1.0 gm. tid	6 months Hysterectomy 4-11-27
5	4-13-27 6- 9-27	JC	1.5	M	Upper Resp. Infection	52 95	5.01 6.12			0.5 gm. tid	3-4 months. Graph No. 3 Health rapidly regained Failure of previous therapy
6	12-31-26 2-20-27 4- 8-27	BP	2	M	Malnutrition Upper Resp. Infection	38 98 100	3.40 5.68 5.86			1 gm. tid 1 gm. stopped	6 months Health rapidly regained Failure of previous therapy
7	4-26-27 5-24-27 6- 1-27	BP	13	F	Unknown Cause	72 96 90	3.92 5.74 5.25			1 gm. tid	1 year Severe menstrual flow

TABLE IV, Continued

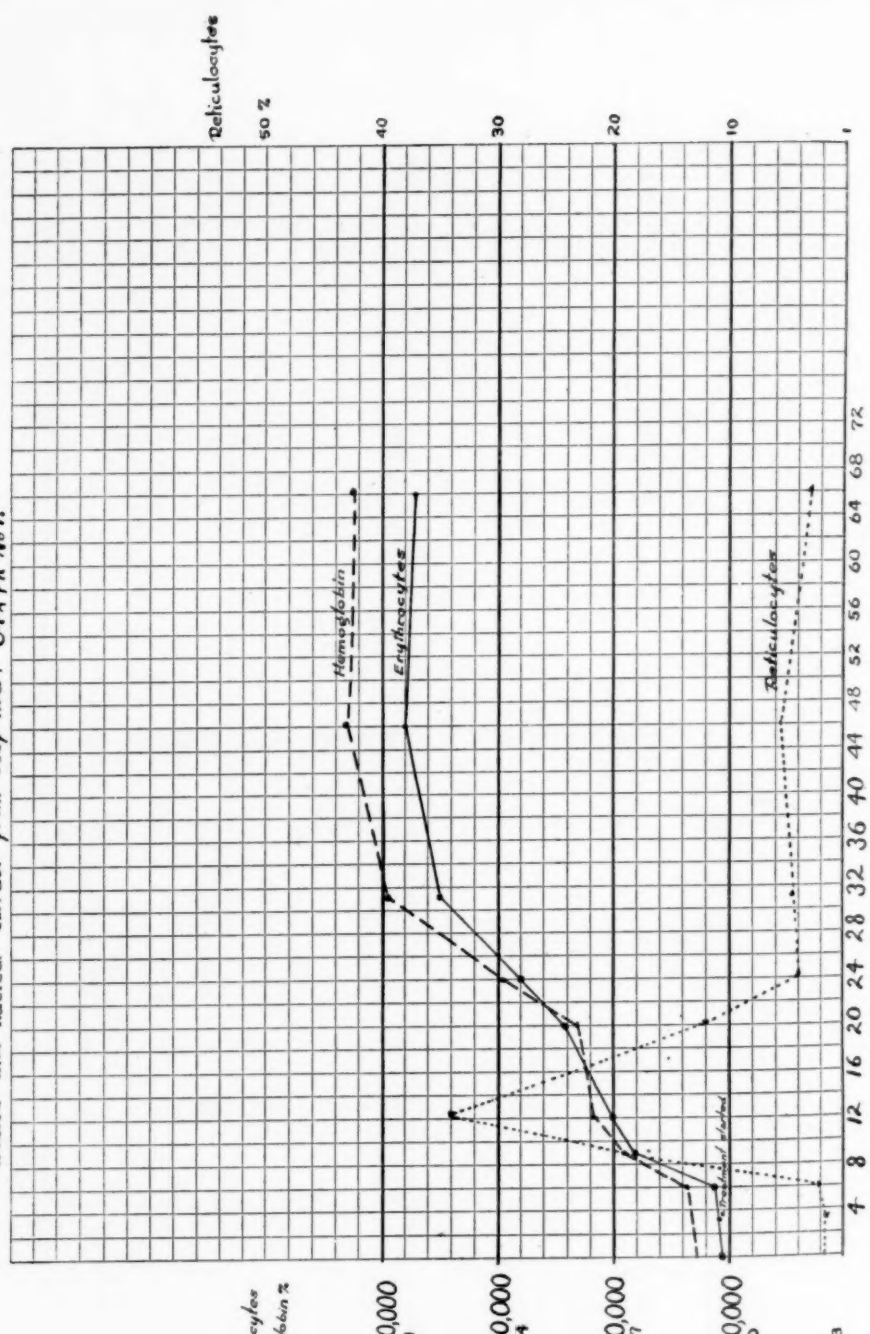
8	5-19-27	W	24	F	Unknown	57	3.95		0.6 gm. tid	2-3 years, periodically
	6- 9-27				Cause	92	5.24			
9	7-18-27	LR	26	F	Hemorrhage	20	1.41		550 cc. whole blood	Acute onset
	7-25-27				Peptic Ulcer	38	2.64		1 gm. tid	
	8-20-27					74	4.42			Gastroenterostomy
	8-22-27					58	3.60			
	9-10-27					94	5.24			Discharged
10	8- 3-27	IW	19	F	Hemorrhage	32	1.95		2 gm. tid	Acute onset
	8-29-27				Abortion	64	3.40			
	9-13-27					95	5.24			Discharged
10-A	8-30-27	Mrs. D	28	F	Hemorrhage	51	2.98	3	Curettement	Acute onset
	9-30-27				Abortion	64	3.89	4		Used as control
	10- 8-27					68	4.00			Discharged
11	2-22-28	CB	47	M	Lobar	111	5.28		2 gm. tid	Anemia following lobar
	3- 6-28				Pneumonia					pneumonia
	3-20-28					48	3.52			Graph No. 2
	4- 2-28					60	4.08	12		
						86	6.08	3		Discharged
12	8- 7-27	LZ	45	M	Cellulitis	48	3.02		2 gm. tid	Anemia following cellulitis
	8-17-27				of Thigh	95	5.14			Discharged

TABLE IV, Continued

13	10-12-27	Martha	1	F	Nutritional	38	2.96	1 gm. tid	Identical twins
	11-14-27				Disturbance	50	4.20		
	1-11-28					55	4.80		
13-A	10-12-27	Mary	1	F	Nutritional	38	3.19	Dietetic tr. only	Used as a control
	11-14-27				Disturbance	40	3.80		
	1-11-28					40	4.70		
14	12- 9-27	FA	22	M	Hemorrhage	19	1.28	500 cc. whole blood	Acute onset
	12-15-27				Peptic Ulcer	30	2.30	2 gm. tid	Marked clinical improvement
	12-20-27					50	3.22		
	1-11-28					75	4.98		
	1-17-28					89	5.24		
14-A	12-20-27	CB	32	M	Pulmonary	40	2.52		Acute onset
	12-23-27				Hemorrhage	36	2.62		Case used as a control
	1-11-28				Cause	40	3.03		
	1-17-28				Unknown	46	3.24		Slow recovery
15	8- 7-27	LZ	21	F	Following	52	3.02	2 gm. tid	Acute onset
	8-10-27				Acute Peri-	84	4.37		
	8-17-27				tonitis	96	5.14		Rapid recovery
15-A	8-26-27	LH	19	F	Acute	30	1.92	Transfused	Acute onset
	8-28-27				Hemorrhage,	40	2.10	whole blood	Used as control
	8-31-27				Abortion	58	2.50		Slower recovery

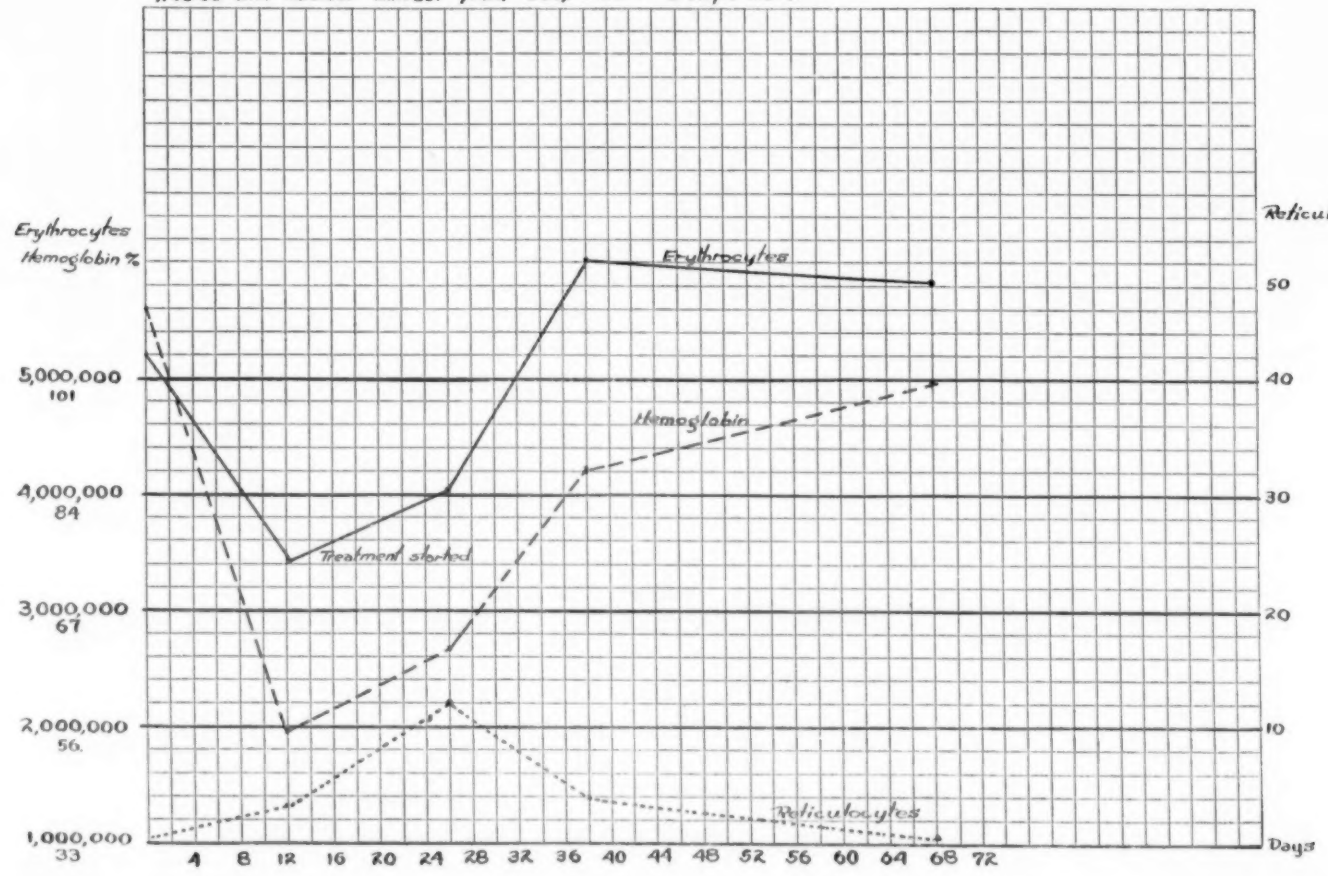
TABLE IV, Continued

16	11- 8-27	FLW	48	F	Hyperplastic Sinusitis	73	4.15			Anemia several years
	11-15-27									Radical antrum operation
	11-30-27					52	3.75		2 gm. tid	Secondary hemorrhage
	12- 5-27					47	2.87			Liver ext. stopped
	12-21-27					69	4.05		liver 1 lb.	Discharged—good recovery
	1-7-28					89	4.65			
16-A	3-20-28	AM	23	F	Purulent Sinusitis	60	4.02	4	Intra-nasal puncture	Acute secondary hemorrhage
	4-20-28					54	4.52	5		Used as control
	5-24-28					72	5.10	3		Slow recovery
17	3-17-28	CZ	63	F	Carcinoma Stomach	48	3.74	6	2 gm. tid for 12 days	Discharged
	4-23-28					44	3.54	3		
	4-30-28					60	4.24		3 gm. tid for 19 days	
	5-12-28					76	4.68		Partial gastrectomy	
18	10- 6-27	AN	25	F	Sickle cell (?)	62	3.75		1 gm. tid	Anemia for at least 10 yrs.
	11-12-27					71	4.02			Graph No. 3
	12-12-27					76	4.35			Severe menorrhagia
	1- 6-28					79	4.48			
	2-22-28					68	3.50			Very fair clinical improvement
	3-22-28					80	4.56			


W.L. - Male. Age 62 - Pernicious Anemia
Treated with nuclear extract from beef liver. Graph No 1.
Reticulocytes
50 %
40
30
20
10
Hemoglobin
Erythrocytes
Reticulocytes
Erythrocytes
Hemoglobin %
5,000,000
101
4,000,000
84
3,000,000
67
2,000,000
50
33
4 8 12 16 20 24 28 32 36 40 44 48 52 56 60 64 68 72
C.B. Male - Age 47 Anemia following lobar pneumonia.

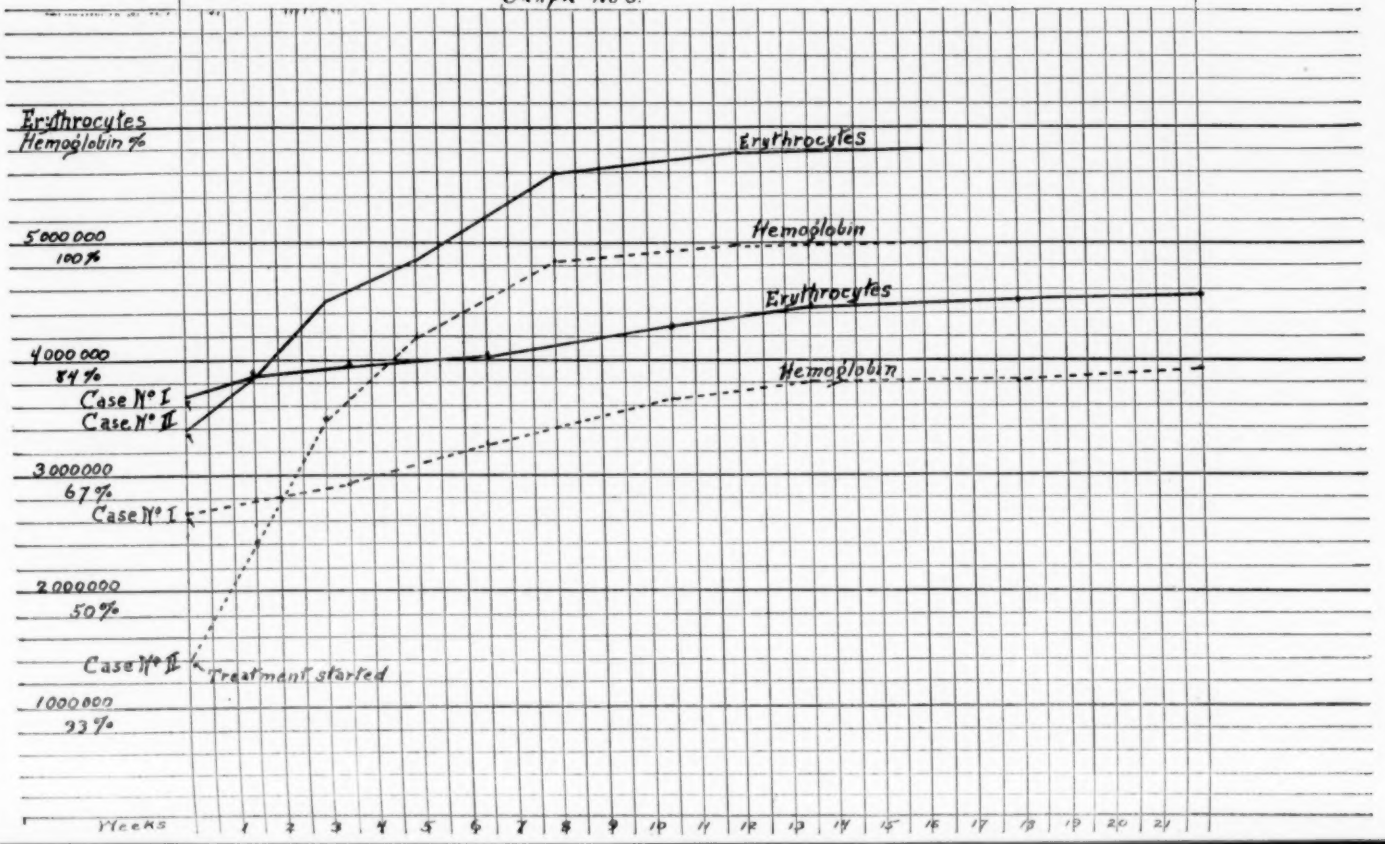
C.B. Male - Age 47 Anemia following lobar pneumonia.

Treated with Nuclear Extract from Beef Liver. Graph No 2.



Case N°I Sickle cell anemia treated with nuclear extract from beef liver
Case N°II Secondary anemia in 18 mo. male due to nutritional error and infection

Graph No. 3.



tween the cause of the anemia operating and the capacity of the hemopoietic centers of the bone marrow to respond to stimulation. Case No. 17, a woman with carcinoma of the stomach, made no gain on 6 gm. nuclear extractives daily in 12 days, but after partial gastrectomy, showed a gain of 32% hemoglobin and 1.14 million red cells on 9 gm. of the same extractives in 19 days. The control cases 10-A, 14-A, 15-A and 16-A might suggest that the patient would not have shown this gain had she not been so treated.

Case No. 18, a young white woman suffering from a chronic anemia which simulated sickle cell anemia (to be reported by Drs. Hunter and Adams from the Department of Pathology, University of Oregon) showed marked clinical improvement under the administration of 1 gm. liver extractives three times daily. Gastrointestinal distress disappeared, the pallor of her skin and mucous membranes became much less marked and the hemoglobin and red cell content progressively increased, over a period of five months, from 62 to 80 per cent and 3.75 million to 4.56 million respectively. Under no other form of treatment had improvement ever been observed.

Nuclear Extractives Obtained from Beef Spleen

Six patients suffering from pernicious anemia have been treated by the use of sodium nucleates and nucleoproteins obtained from beef spleen. A resumé of their data is given in table V. Graph No. 4 illustrates the progress under treatment of patient No. 1. Two patients present the same initial rise in reticulocyte count, the rapid gain in hemoglobin and red blood cell content, and the same clinical improvement observed from high liver feeding. Patients No. 2 and 3 had previously eaten liver, and the increase of the reticulated cells was delayed and less high than in patients Nos. 1 and 4 who had not eaten liver. Patient No. 2 was given spleen extractives, 9 gm. for 4 days and 12 gm. for 14 days, with a rise of 15% hemoglobin; then liver extractives 9 gm. for 15 days, with a rise of 22% hemoglobin; then spleen extractives 9 gm. for 9 days with a rise of 5% hemoglobin, at which time she returned home on liver feeding. Patient No. 3 was given 9 gm. spleen extractives for 14 days and showed a gain of 14% hemoglobin; then 9 gm. liver extractives for 4 days with a gain of 5% hemoglobin, then for 10 days, 9 ounces of raw liver was given, with a gain of 4% hemoglobin, and finally for a period of 21 days 3 vials of Lilly's liver extract were added to the 9 ounces of raw liver with a gain of 5% hemoglobin. The numbness and tingling of the hands and feet, from which this patient suffered, did not disappear. We have seen the paresthesia disappear twice in pernicious anemia patients; once from liver feeding and once from the use of the nuclear extractives obtained from spleen. For the most part, however, we have seen no effect upon the symptoms of cord lesions.

Discussion. In presenting at this time this brief report of our clinical observations on the use of nuclear extractives obtained from different ani-

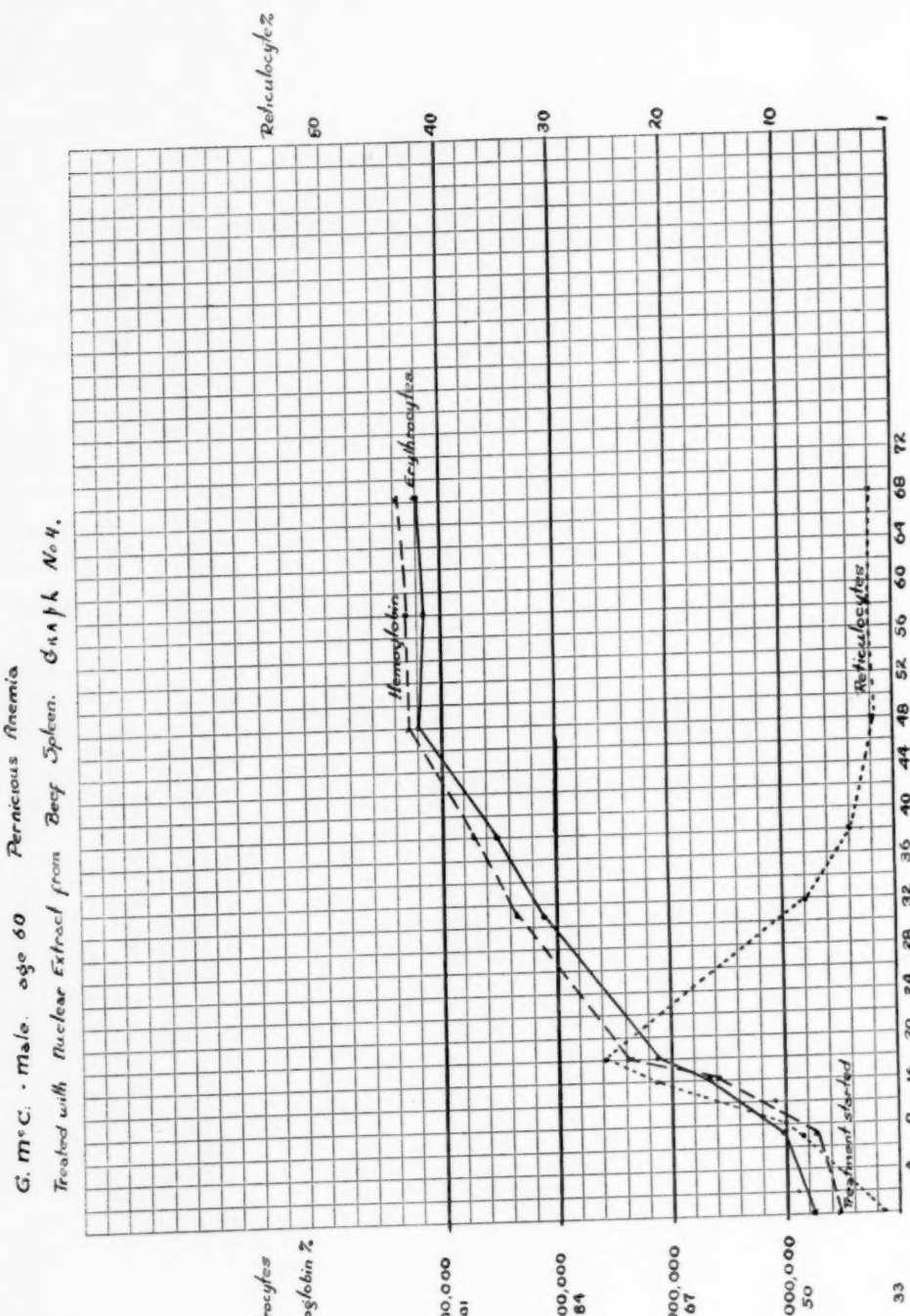
SODIUM NUCLEATE AND NUCLEOPROTEIN FROM SPLEEN
CASES OF PRIMARY ANEMIA

TABLE V

No.	Date	Name	Age	Sex	Diagnosis	Hb. %	RBC	Retic. %	V.I.	Therapy	Duration of Anemia Remarks
1	3-14-28	NMcC	58	M	Pernicious	56	2.16	1.4	1.18	3 gm. tid	Duration 3 years
	3-17-28				Anemia	66	2.80	20.			Graph No. 4
	3-20-28					70	3.00	34.			
	3-28-28					75	3.41	12.			
	4- 4-28					83	3.80	4			Marked clinical improve-
	4-11-28					100	4.50	4.5			ment
2	3-29-28	KMcC	70	F	Pernicious	47	1.80	0.1	1.34	3 gm. tid	Duration 5 years
	4- 2-28				Anemia	55	1.94	2.0		4 gm. tid	Had previously eaten liver
	4- 9-28					54	1.96	6.6			Marked clinical improve-
	4-16-28					62	2.18	11.0		3 gm. tid liver ext.	ment
	4-27-28					79	3.20	6.0		(replaced spleen)	
	5- 1-28					84	3.14	4.0		3 gm. tid spleen ext.	
	5- 9-28					89	3.15	2.0		(replaced liver)	
3	4- 2-28	EPL	54	F	Pernicious	69	2.59	0.2	1.36	3 gm. tid	Duration 2 years
	4- 6-28				Anemia	77	3.00	0.4		3 gm. liver ext.	Had previously eaten liver
	4-11-28					80	2.86	2.2		tid (replaced spleen)	and taken Lilly's liver ext.
	4-16-28					83	3.33	1.0		9 oz. raw liver daily	Some general improve-
	4-20-28					87	2.96	2.4		(replaced liver ext.)	ment—Numbness of ex-
	4-25-28					85	2.89	3.2		3 vials Lilly's liver	tremities continues
	4-30-28					91	3.33	3.7		ext. added to raw	
	5- 4-28					93	3.42	3.0		liver	
	5-21-28					96	3.70	1.9			

TABLE V, Continued

4	4-22-28	AA	72	F	Pernicious	58	1.86	1.6	1.52	3 gm. tid	Duration (?)
	4-30-28				Anemia	66	2.37	11.0			
	5- 8-28					74	3.06	14.0			Marked clinical improve-
	5-22-28					90	4.03	8.0			ment
5	6-15-28	GP	72	F	Pernicious	28	0.90	7.8	1.22	3 gm. tid	Duration several months
	6-21-28				Anemia	33	1.40	10.0			Marked clinical improve-
	6-29-28					46	2.46	9.0			ment
6	5-21-28	ST	55	F	Pernicious	45	1.80	1.0	1.17	3 gm. tid	(Started 5-25-28)
	6- 1-28				Anemia	58	1.96	4.0	1.14		Marked parasthesias
	6-15-28					64	2.21	13.4			All parasthesias gone
	6-21-28					80	3.42	7.0			Marked clinical improve-
	6-29-28					84	3.49	5.0			ment


G. M°C. - Male. age 60 Pernicious Anemia
Treated with Nuclear Extract from Beef Spleen. Graph No 4.
Reticulocyte %
Hemoglobin
Erythrocytes
Reticulocytes
Treatment started
Erythrocytes
Hemoglobin %
5,000,000
101
4,000,000
84
3,000,000
67
2,000,000
50
33
60
40
30
20
10
1
4 8 16 20 24 28 32 36 40 44 48 52 56 60 64 68 72

mal sources in the treatment of human anemias, we have been actuated mainly by the fact that our experience is at variance with the clinical reports thus far published by others. The experimental work of Leake, Bacon and Evans, Robscheit-Robbins and Whipple and by ourselves (5), and the results obtained by McCann (6), all point to the belief that there are one or more factors common to bone marrow, spleen, liver, chicken blood cells, kidney, etc., which have similar hemopoietic effects upon the animal body. Nuclear extractives are common to all of these substances. The facts that such extractives obtained from the washed nuclei of chicken blood cells have this hemopoietic stimulant effect markedly and that the cytoplasm of the blood cell does not possess it at all are especially suggestive.

If we can tentatively conclude anything from our limited work, both clinical and experimental, it is that the hemopoietic stimulant, unknown as yet as to its composition, is an integral part of the cell nucleus, and that the effect noted upon blood production from the taking of different animal tissues depends upon the amount of nuclear substance contained in that particular meat eaten. Liver has shown, in our experimental work, a greater stimulant effect than pancreas and thymus, but less than that of spleen; and the greatest effect, thus far noted, has been obtained from the washed nuclei of the blood cells from the fowl. A practical point may be suggested from this observation, namely, that liver alone, which is often repugnant to persons, may be replaced by the eating of kidney, sweetbreads, spleen and possibly beefsteak. The use of expensive pharmaceutical products may therefore be in part avoided.

One more point of importance seems to be logically deduced from our work. The results indicate a like response from the administration of these nuclear extractives in both primary and secondary anemias. Modifying factors may enter both groups and prevent or alter type blood reactions.

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(3) J. A. M. A., 1928, xc:75-78.

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(5) Cited and reported: J. A. M. A., 1928, xc:75-78.

(6) Proc. Soc. Exp. Biol. & Med., 1928, xxv:255.

A Study of the Differential Blood Count in One Thousand Cases of Active Pulmonary Tuberculosis*

By John W. Flinn, *Prescott, Arizona*

THIS study was prompted by the work of Cunningham, Sabin et al, at the Johns Hopkins Hospital, on the rôle of the monocyte in experimental tuberculosis. After the study was begun, its scope was influenced very materially by the conclusions of Medlar and his co-workers at the University of Wisconsin, regarding the different parts played by the monocyte, the neutrophile and the lymphocyte in the histopathological reaction in tuberculosis.

Sabin and her associates, using supravital staining methods, traced the monocyte from its origin in the reticular cells of the spleen and of the bone-marrow to its consummation in the typical epithelioid cell of tuberculosis. As a result of a long series of observations in experimental tuberculosis they "think that a tuberculous process involves a marked new production and proliferation of monocytes in the tissues and their transformation into epithelioid cells."

Incidentally, they found that the transitional cell of the Ehrlich classification is in reality a more mature form of mononuclear cell and is properly classed with the monocytes.

These investigators have also found that they "can quite accurately follow the course of the disease," in rabbits, "by the relative proportions of monocytes and lymphocytes in the circulating blood. When the animals have been killed at the time when the monocytes were markedly above the lymphocytes" they "have consistently found an extensive and active tuberculosis. In animals in which the tuberculosis had not become widespread, or in which the course of the disease was arrested as proved by autopsy" they "have found the lymphocytes in the circulating blood to be much more numerous than the monocytes."

Medlar and Kastlin in their experimental work corroborate the view that the monocyte "plays the chief rôle in the formation of the primary mononuclear or epithelioid tubercle." In addition, they made a very careful study of the part played by the polymorphonuclear leucocyte—the neutrophile—in the tissue reaction to the tubercle bacillus. They found this neutrophilic cell attracted to the scene of action after the monocytes had

*Presented before the American College of Physicians, New Orleans, March 6, 1928.

undergone necrosis, following an unsuccessful attempt to combat the infection. These neutrophiles, through their proteolytic enzymes tend to liquefy the necrotic material and give rise to suppuration. If the neutrophiles are killed, incomplete digestion of the dead connective tissue ensues and typical caseous material results.

These workers found that the lymphocytes are the cells principally concerned with healing in tuberculosis. If the healing occurs early with destruction of the tubercle bacilli, lymphocytes alone take part. If, however, healing occurs later, after suppuration and caseation have taken place, the lymphocytes are apparently aided by the monocytes in the healing process. It was the conclusions of these investigators that induced us to include the neutrophiles in this study.

Our first reaction to the findings of Cunningham, Sabin et al, regarding the monocyte-lymphocyte ratio in the circulating blood of tuberculous animals was a desire to investigate this ratio in tuberculosis in man. Our thought was to carry on a series of observations on routine patients, using supravital staining methods. We found these methods so time-consuming, however, that we were forced to abandon this plan.

It then occurred to us to use the records, which have been accumulating in our office for many years, of routine blood examinations of patients in all stages of pulmonary tuberculosis, and to make an intensive study of the blood-picture in one thousand of these patients. It is true that these counts were made from fixed films stained with Wright's stain, but we believe they are sufficiently accurate for practical purposes. Using these records gave us access to a much larger number of cases than we could possibly accumulate in a short time. Moreover, since these were routine counts, by different technicians, made with no thought of proving anything in particular, they probably represent a fairly accurate cross-section of typical blood pictures in active pulmonary tuberculosis.

We were soon faced with the question whether a consideration of the percentages of monocytes, neutrophiles and lymphocytes was sufficient, or whether it was advisable to calculate the numbers of these cells per cubic millimeter. This seemed to us a rather important question, since percentages can be calculated from dried films which can, if necessary, be sent to a distant laboratory; while total white counts and numbers of monocytes, neutrophiles and lymphocytes per cu. mm. can be made only from freshly drawn blood specimens.

Finally we compromised between these two positions. We took the blood pictures from three hundred and fifty cases examined in the war period when laboratory technicians were scarce, and when we were forced to send blood specimens to a laboratory in a distant town. In these we have only the percentages of monocytes, neutrophiles and lymphocytes recorded, and the conclusions in these three hundred and fifty cases are based solely on these percentages. Over against these we placed the records of six hundred and fifty cases in which the blood counts were made

in our own laboratory and included total leucocyte counts and numbers and percentages of monocytes, neutrophiles and lymphocytes.

In our monocyte count we included the large and the small mononuclears and the transitionals of the Ehrlich classification. Neither the eosinophiles nor the basophiles are included in this study.

In the classification of cases we used the plan adopted by the National Tuberculosis Association as a basis. The first two divisions of this classification were adopted as outlined—the minimal and the moderately advanced. From the third class—far advanced—of the National Tuberculosis Association, a fourth class—"very far advanced—probably hopeless" was taken. This gave us four classes: I Minimal. II Moderately Advanced. III Far Advanced. IV Very far Advanced, probably hopeless.

Chart I shows the average numbers of monocytes, neutrophiles and lymphocytes per cubic millimeter in each of the four different classes of the six hundred and fifty-one cases of the second part of this study. It also records the monocyte-lymphocyte ratio and the lymphocyte-neutrophile ratio in these different averages. These calculations included twelve hundred and forty-six blood counts in six hundred and fifty-one cases. In class I, the minimal class, there were 125 cases and 215 blood counts. In class II, the moderately advanced class, there were 257 cases and 565 blood counts. In class III, the far advanced—probably hopeless—class—there were 49 cases and 76 blood counts.

The average monocyte count per cubic millimeter was 159 in the minimal class. It increased to 183 in the moderately advanced class, to 340 in the far advanced, and to 516 in the very far advanced class. In other words the average monocyte count per cu. mm. *increased* steadily until it was 3¼ times greater in the very far advanced cases, than in those cases showing only a minimal lesion.

The average neutrophile count per cubic millimeter was 4161 in the minimal class. It increased to 5055 in the moderately advanced class; to 6952 in the far advanced class; to 8880 in the very far advanced class. In other words the average neutrophile count per cu. mm. *increased* steadily until it was more than 2 1/10 times greater in the very far advanced cases than in the minimal class.

The average lymphocyte count per cu. mm. was 2664 in the minimal class. It increased to 2898 in the moderately advanced class and then decreased to 2781 in the far advanced class. It decreased still further—to 2460—in the very far advanced class. In other words the average lymphocyte count per cu. mm. did not vary nearly so greatly and not so consistently as did the average monocyte and the average neutrophile counts.

The average percentage of monocytes increased from 2.1% in the minimal class to 2.9% in the moderately advanced class. It further increased to 3.3% in the far advanced class, and to 4.3% in the very far advanced class. In other words the average percentage of monocytes was

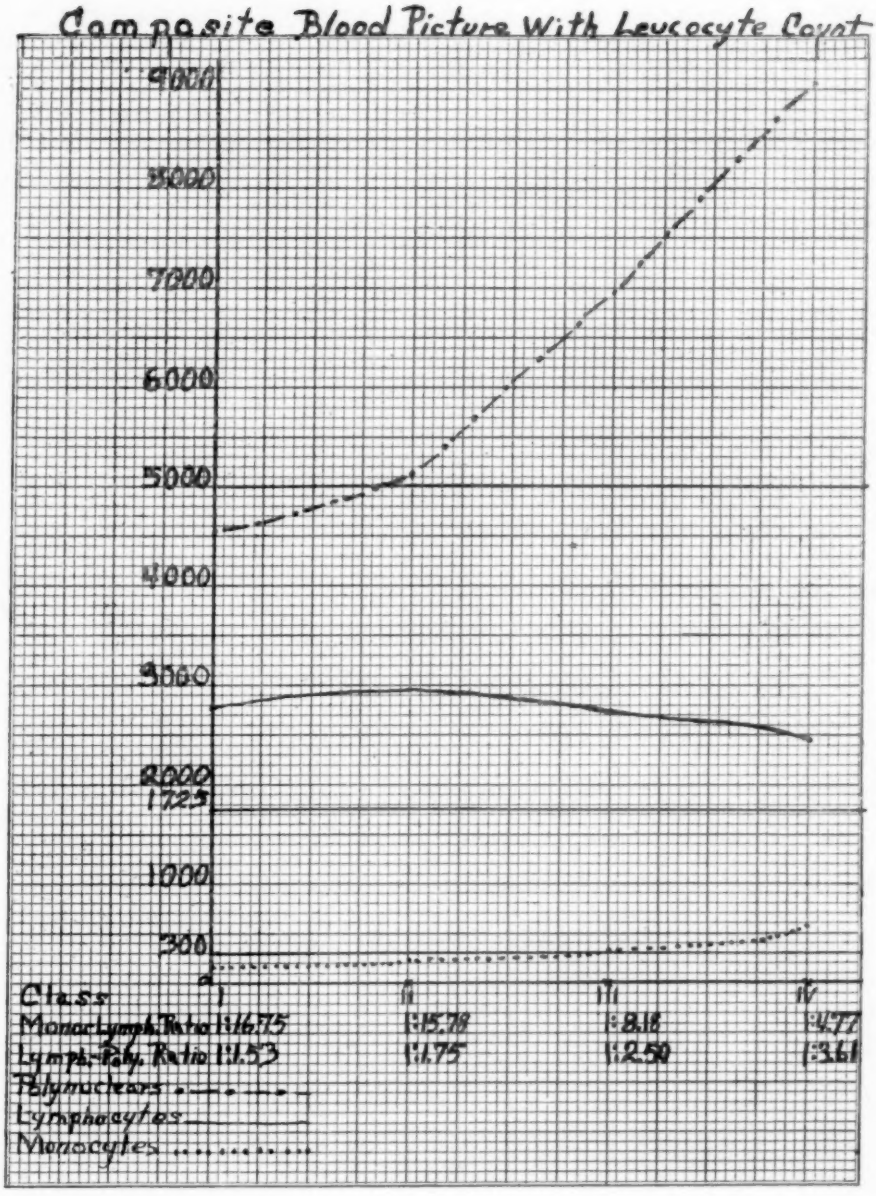

Composite Blood Picture With Leucocyte Count
9000
8000
7000
6000
5000
4000
3000
2000
1725
1000
300
Class I II III IV
Mono-Lymph. Ratio 1:16.75 1:15.78 1:8.18 1:4.77
Lymph.-Poly. Ratio 1:1.53 1:1.75 1:2.50 1:3.61
Polymacleors
Lymphocytes
Monocytes

CHART I

more than twice as great in the fourth class as in the first class.

The lymphocytes decreased from 36.3% in Class I to 34.5% in Class II; to 27.2% in Class III, and to 20.5% in Class IV. In other words the average percentage of lymphocytes decreased steadily and markedly until the percentage in the far advanced cases was down nearly to one half the percentage in the minimal cases. In general there was a noticeable increase in the percentages of both monocytes and neutrophiles and a more marked decrease in the percentage of lymphocytes as these cases progressed from the minimal to the very far advanced stage.

The average monocyte-lymphocyte ratio and the average lymphocyte-neutrophile ratio calculated from the cubic millimeter counts in these 651 cases showed more marked changes in each class, than did either the average total cubic millimeter count or the average percentage calculation. The average monocyte-lymphocyte ratio in Class I was 1:16.75; in Class II it was 1:15.78; in Class III 1:8.18; and in Class IV 1:4.77. In other words the ratio of lymphocytes to monocytes had decreased in the very far advanced cases to almost one quarter of what it was in the minimal cases. The average lymphocyte-neutrophile ratio in Class I was 1:1.53; in Class II it was 1:1.75; in Class III 1:2.50, and in Class IV 1:3.61. In other words the ratio of neutrophiles to lymphocytes increased in the very far advanced cases to more than 2½ times greater than in the minimal cases.

To summarize the results of the study of the average counts in the 651 cases in which the blood counts were made in our own laboratory and included total lymphocyte counts and numbers and percentages of monocytes, neutrophiles and lymphocytes:

(1) The average number of monocytes and neutrophiles per cu. mm. increases noticeably as the disease becomes more advanced; the increase in monocytes being proportionately the greater increase of the two.

(2) The average number of lymphocytes per cu. mm. at first increases slightly as the disease advances. It then slowly decreases and towards the end decreases quite rapidly.

(3) The average percentages of monocytes and of neutrophiles increase noticeably as the disease becomes more advanced, the increase in the percentage of monocytes being proportionately the greater of the two.

(4) The average percentage of lymphocytes decreases very noticeably as the disease becomes more advanced, the decrease being almost as great proportionately as is the increase in monocytes.

(5) The most marked changes are found in the monocyte-lymphocyte and the lymphocyte-neutrophile ratios, as calculated from the cu. m.m. counts. The monocyte-lymphocyte ratio decreases very considerably as the disease becomes more advanced, while the lymphocyte-neutrophile ratio increases almost as greatly.

Chart II. shows the average percentages of monocytes, neutrophiles and lymphocytes in each of the four different classes in 345 cases of the first part of this study. It also re-

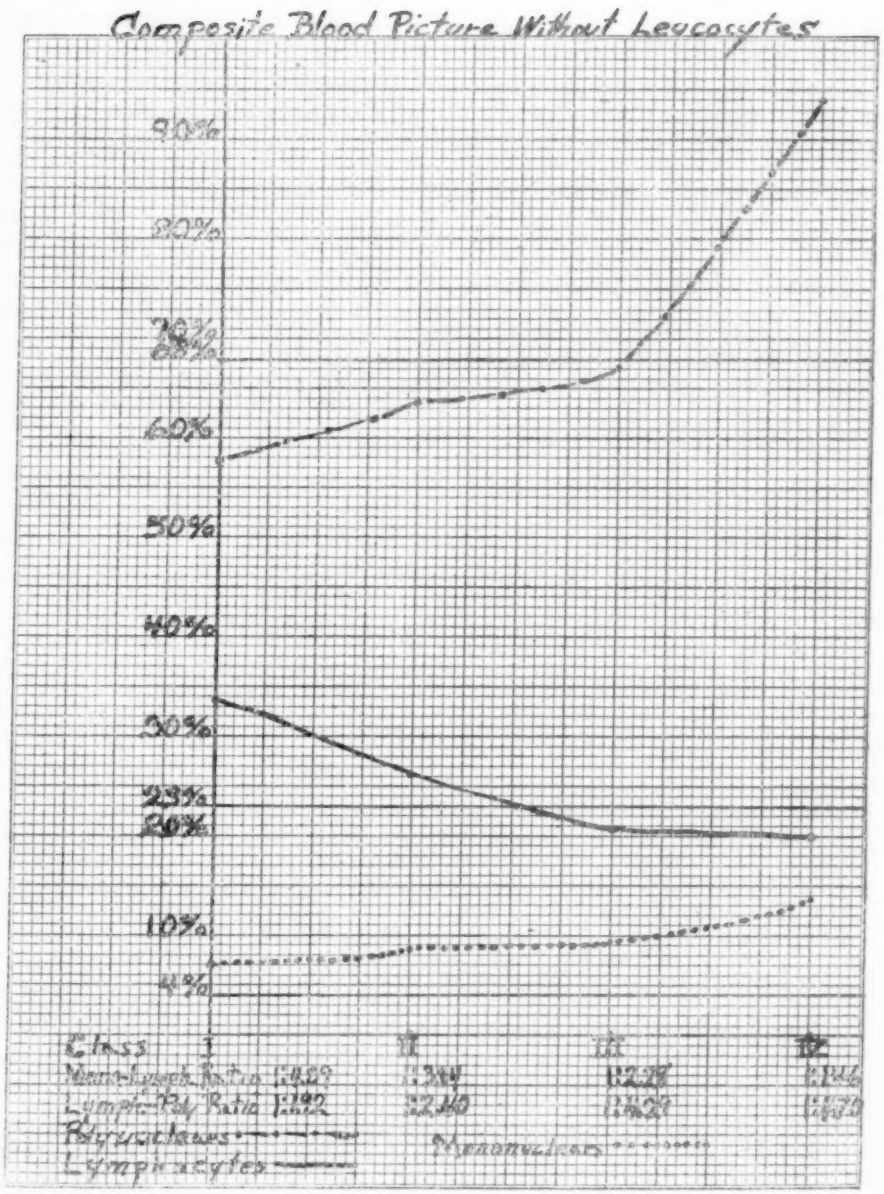

Composite Blood Picture Without Leucocytes
90%
80%
70%
60%
50%
40%
30%
23%
20%
10%
4%
Class I II III IV
Myelocytes
Lymphocytes

CHART II

cords the monocyte-lymphocyte ratio and the lymphocyte-neutrophile ratio in these different averages.

These calculations include 632 blood counts in 345 cases. In Class I—the minimal class—there were 35 cases and 59 blood counts; in Class II—the moderately advanced class—there were 163 cases and 298 blood counts; in Class III—the far advanced class—there were 140 cases and 266 blood counts; in Class IV—the very far advanced, probably hopeless class—there were seven cases and nine blood counts.

The average percentage of monocytes was 7.6% in the minimal class. It *increased* to 8.3% in the moderately advanced class; to 9.1% in the far advanced class, and to 13.7% in the very far advanced class. In other words the average percentage of monocytes increased steadily until in the fourth class this percentage was almost double what it was in Class I.

The average percentage of neutrophiles was 57.9% in Class I. It increased to 63.5% in Class II; to 68.9% in Class III, and to 94% in Class IV. In other words the average percentage of neutrophiles increased steadily until in the fourth class this percentage was more than 50% greater than in Class I.

The average percentage of lymphocytes was 33.9% in Class I. It decreased to 26.4% in Class II; to 20.7% in Class III, and to 20% in Class IV. In other words the average percentage of lymphocytes decreased steadily until in the fourth class it was more than 33% less than in Class I.

The monocyte-lymphocyte ratio and the lymphocyte-neutrophile ratio showed even more marked changes in this series also. The monocyte-lymphocyte ratio was 1:4.09 in Class I. It *decreased* to 1:3.14 in Class II; to 1:2.28 in Class III; and to 1:1.46 in Class IV. The lymphocyte-neutrophile ratio was 1:1.92 in Class I; *increased* to 1:2.40 in Class II; to 1:4.29 in Class III and to 1:4.70 in Class IV.

The summary of the results in the average percentages and in the monocyte-lymphocyte and the lymphocyte-neutrophile ratios in the previous series of 651 cases applies equally well to this series of 345 cases in which only differential counts on dried films were made. This striking similarity of results seems all the more remarkable when the noticeably different percentages of monocytes and of lymphocytes in the same classes in the two series of cases is observed. This was evidently due to different systems of identifying different mononuclear cells. The technicians in the series of 345 cases undoubtedly classified many cells as monocytes which those who examined the blood in the 651 cases identified as lymphocytes. And yet, as noted above, the averages correspond very closely.

Chart III shows three differential blood counts on a far advanced case of pulmonary tuberculosis which improved rather remarkably under quite prolonged bed-rest and subsequent very carefully graduated exercise. In May 1925 this patient had extensive active involvement in all lobes of one lung with rather slight active disease in the upper lobe of the other lung. At that time she had a very high

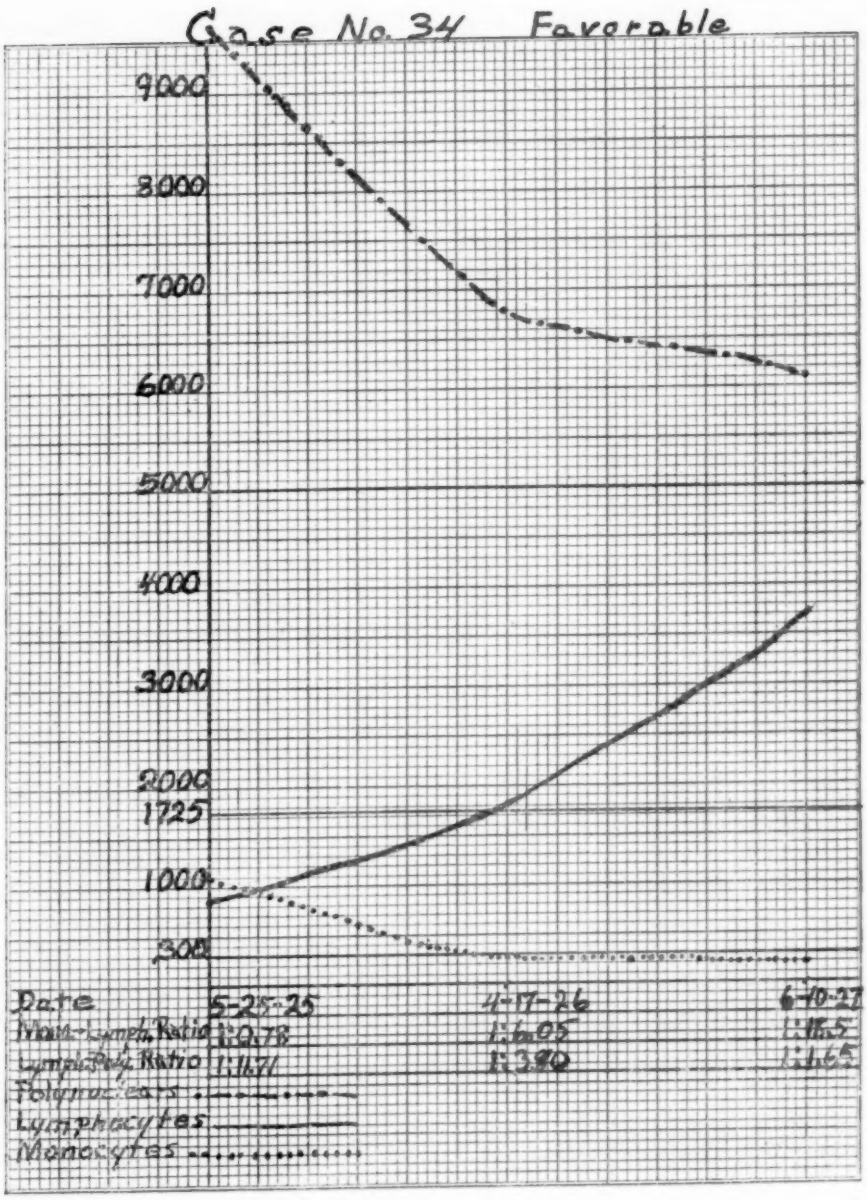

Case No. 34 Favorable
9000
8000
7000
6000
5000
4000
3000
2000
1725
1000
300
Date
5-25-25
4-17-26
6-10-27
Mono-Lympho. Ratio 1:0.78
1:1.05
1:1.15
Lympho-Poly. Ratio 1:1.71
1:3.90
1:1.65
Polymorphocytes
Lymphocytes
Monocytes

Chart III

monocyte count (above 1,000 per cu. mm.) a very high neutrophile count (above 9,000) and a very low lymphocyte count (below 1,000). After one year's rest in bed her lung condition and symptoms had improved rather markedly. At the same time the monocytes and neutrophiles had noticeably decreased and there had been a similar increase in the number of lymphocytes. At the end of another year, spent on very carefully graduated exercise, the symptoms had disappeared, the lung condition was almost quiescent and the leucocytic picture showed still further improvement. Corresponding changes are noted in the monocyte-lymphocyte and in the lymphocyte-neutrophile ratios.

In this case—an exceptionally favorable one—the leucocytic picture runs absolutely true to the form laid down in the composite graphs. The monocytes and the neutrophiles decrease steadily and consistently from beginning to end, and the lymphocyte-neutrophile ratio shows a corresponding *decrease*. On the other hand a similar *increase* is seen in the lymphocyte count and in the monocyte-lymphocyte ratio.

Chart IV shows a more complicated blood-picture in a case which ran a stormy and uncertain course for some time before finally settling down to a fairly satisfactory improvement. This case was admitted in May 1924 with extensive involvement of the right lung throughout, and a history of sudden onset and rapid extension of the disease. One month's rest in bed produced some slight improvement in the symptoms and in the lung findings. This was accompanied by a very satisfactory decrease in the monocyte and the neutrophile counts, and a slight decrease in the lymphocyte-neutrophile ratio. The lymphocyte count, however, did not increase, but it decreased somewhat. The monocyte-lymphocyte ratio too was quite unsatisfactory. Instead of increasing, it decreased to less than one-half.

For the next five months (June to November) this patient did rather badly. The symptoms grew slowly worse and the lung signs increased. During this period the neutrophile count increased greatly. The monocyte count varied with a distinct general trend upward. The lymphocyte count at first increased somewhat and then took a marked drop. The monocyte-lymphocyte ratio increased and then decreased somewhat. The lymphocyte-neutrophile ratio increased greatly.

During the next six weeks (November to January) the patient's symptoms improved, but examination of the chest showed slight activity in the upper lobe of the left lung. It is noticeable that during this period the monocyte count increased although the leucocyte picture improved in every other respect. We then did a successful artificial pneumothorax after which the patient made uncertain but fairly satisfactory improvement. Today she is quite free of symptoms with the lung still compressed.

Chart V shows a leucocytic picture which runs true to form in every respect, except one—the lymphocyte count has not increased satisfactorily. This patient first came under observation in October 1927 with extensive

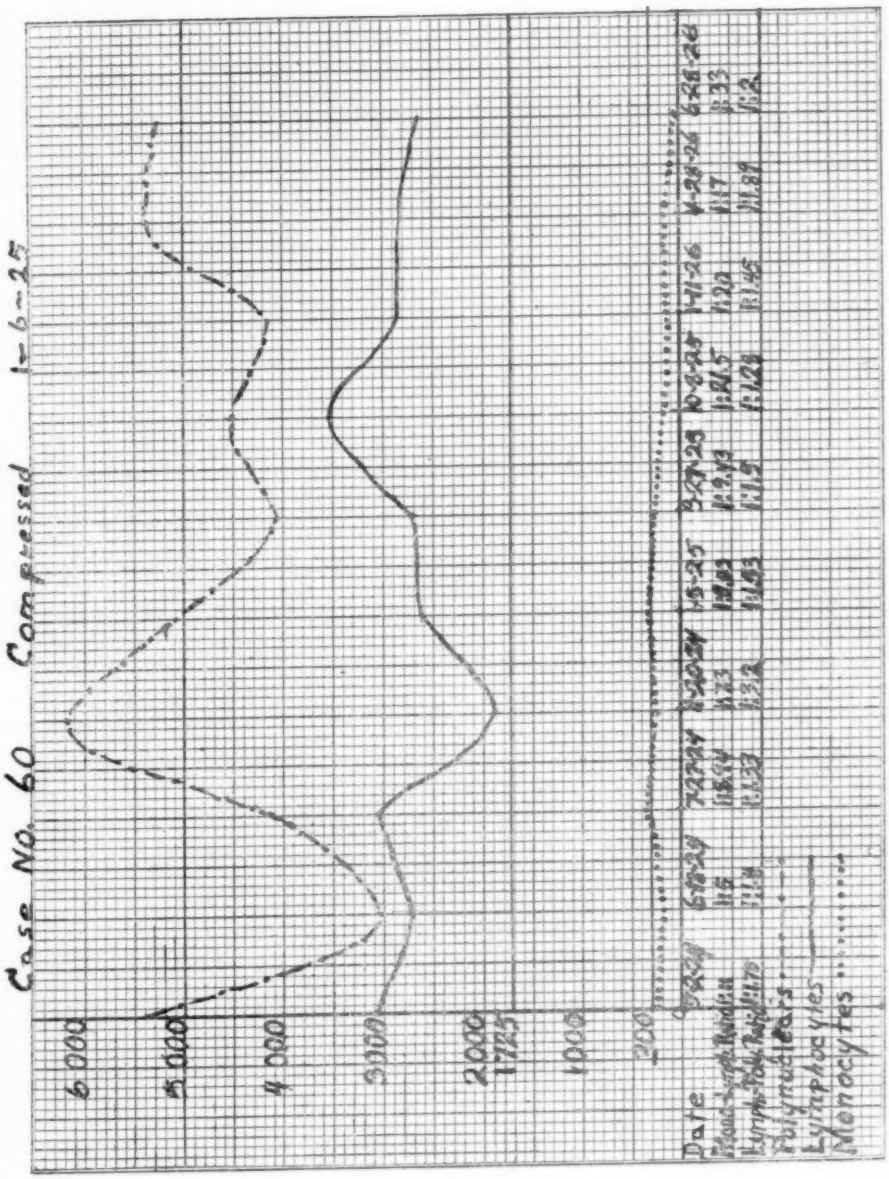

Case No. 60 Compressed In 6-25
6000
5000
4000
3000
2000
1725
1000
200
Date
Polymorphs
Lymphocytes
Monocytes

CHART IV

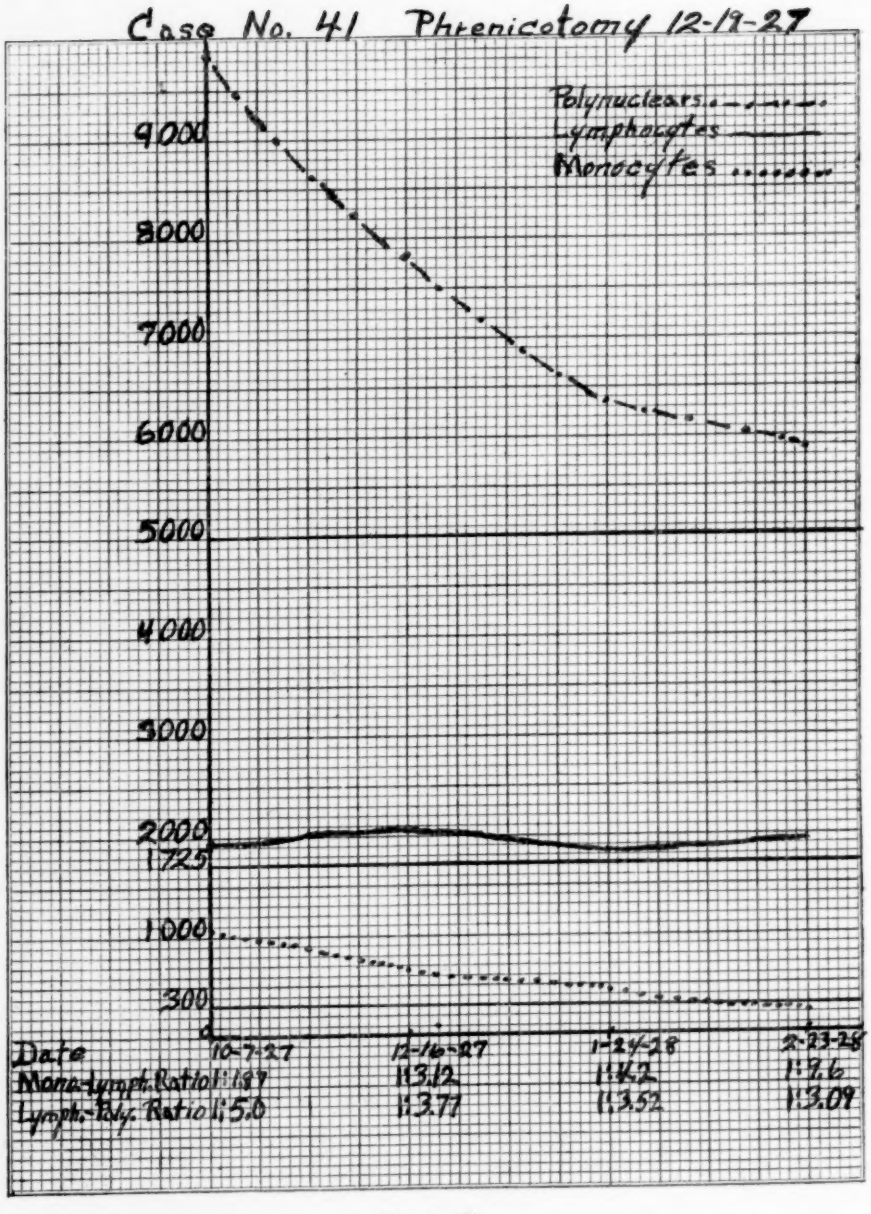

Case No. 41 Phrenicotomy 12-19-27
Polynuclears
Lymphocytes
Monocytes
9000
8000
7000
6000
5000
4000
3000
2000
1725
1000
300
0
Date
10-7-27
12-16-27
1-24-28
2-23-28
Mono-Lymph. Ratio 1:1.87
1:3.12
1:4.2
1:7.6
Lymph.-Poly. Ratio 1:5.0
1:3.71
1:3.52
1:3.09

CHART V

involvement in the right lung throughout. In addition she had very slight low grade active disease in the left upper lobe and the laryngologist reported a suspicious throat. We at once attempted an artificial pneumothorax, but failed after repeated attempts. We then did a right phrenicotomy, since when the patient has improved noticeably, under fairly complete bed-rest. We still consider the outlook for this case doubtful and are inclined to think that a thoracoplasty will be indicated.

Chart VI shows the leucocytic picture of a quite acute case of far advanced unilateral pulmonary tuberculosis which came under observation in February 1925 and ran an unsatisfactory course, under bed-rest, for a full year. In the meantime pneumothorax was attempted, but unsuccessfully. At the end of a year a thoracoplasty was performed, although it did not seem to be a very suitable case for this operation. Since then her condition has improved fairly satisfactorily. Since the thoracoplasty there has been a satisfactory *decrease* in the monocyte count, the neutrophile count and the lymphocyte-neutrophile ratio. There has also been a satisfactory increase in the monocyte-lymphocyte ratio. The increase in the lymphocyte count, however, has not been quite satisfactory. We expect a permanent improvement in this case, but consider it doubtful if the disease will ever become quite quiescent.

Chart VII shows the pictures of a very far advanced case of pulmonary tuberculosis which was classed as probably hopeless when the patient first came under our observation in May 1927. The striking feature of this graph is the steady and persistent increase in the monocyte count with a corresponding decrease in the lymphocyte count, until these two counts are nearly equal at the time of the last examination. This is indicated too by the fact that the monocyte-lymphocyte ratio has decreased from 1:35 to 1:1—nearly thirty-five fold. The neutrophile count in this case is fairly characteristic, as is also the lymphocyte-neutrophile ratio.

Conclusions

1. A full leucocytic picture, including total numbers per cubic millimeter, and percentages of monocytes, neutrophiles and lymphocytes is a very important part of every examination of a tuberculous patient. This information is *always* very helpful in diagnosis, prognosis and treatment, and often gives a truer conception of the pathology of the case than any other part of the examination.

2. The monocyte-lymphocyte and the lymphocyte-neutrophile ratios (of either the numbers per cu. mm. or of the percentages) seem to us to give the truest conception of the status and progress of the case. The percentages in themselves seem the next most reliable indication. The numbers per cubic millimeter although interesting and helpful, seem to us the least important of these three classes of observations.

3. A decreasing monocyte-lymphocyte ratio and an increasing lymphocyte-neutrophile ratio point very definitely to a more active and extensive lesion. The converse points just as

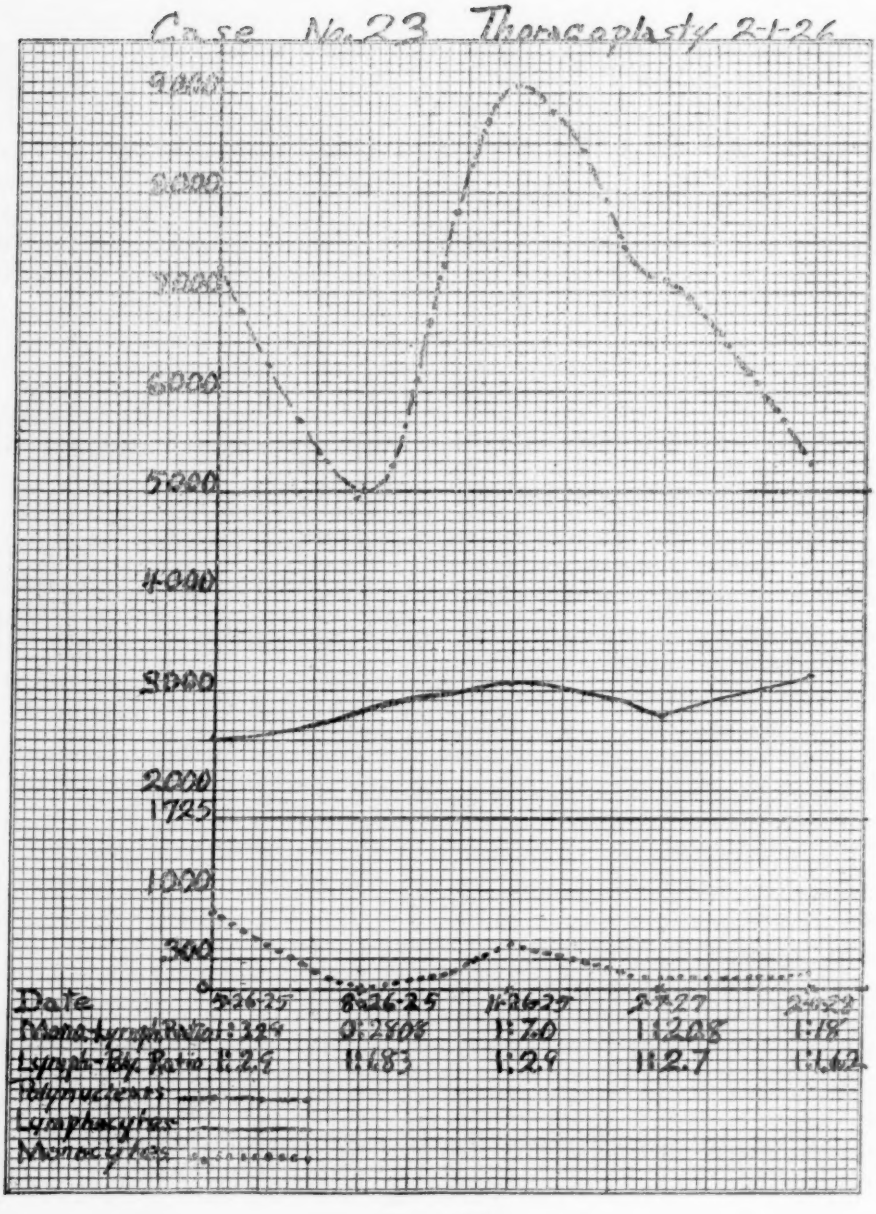

Case No. 23 Thoracoplasty 2-1-26
9000
8000
7000
6000
5000
4000
3000
2000
1725
1000
300
Date
8-26-25
11-26-25
2-27
2-28
Mono-Lymph Ratio 1:3.4
1:2806
1:7.0
1:2.08
1:18
Lymph-Poly Ratio 1:2.6
1:1.83
1:2.9
1:2.7
1:1.62
Polymucleers
Lymphocytes
Monocytes

CHART VI

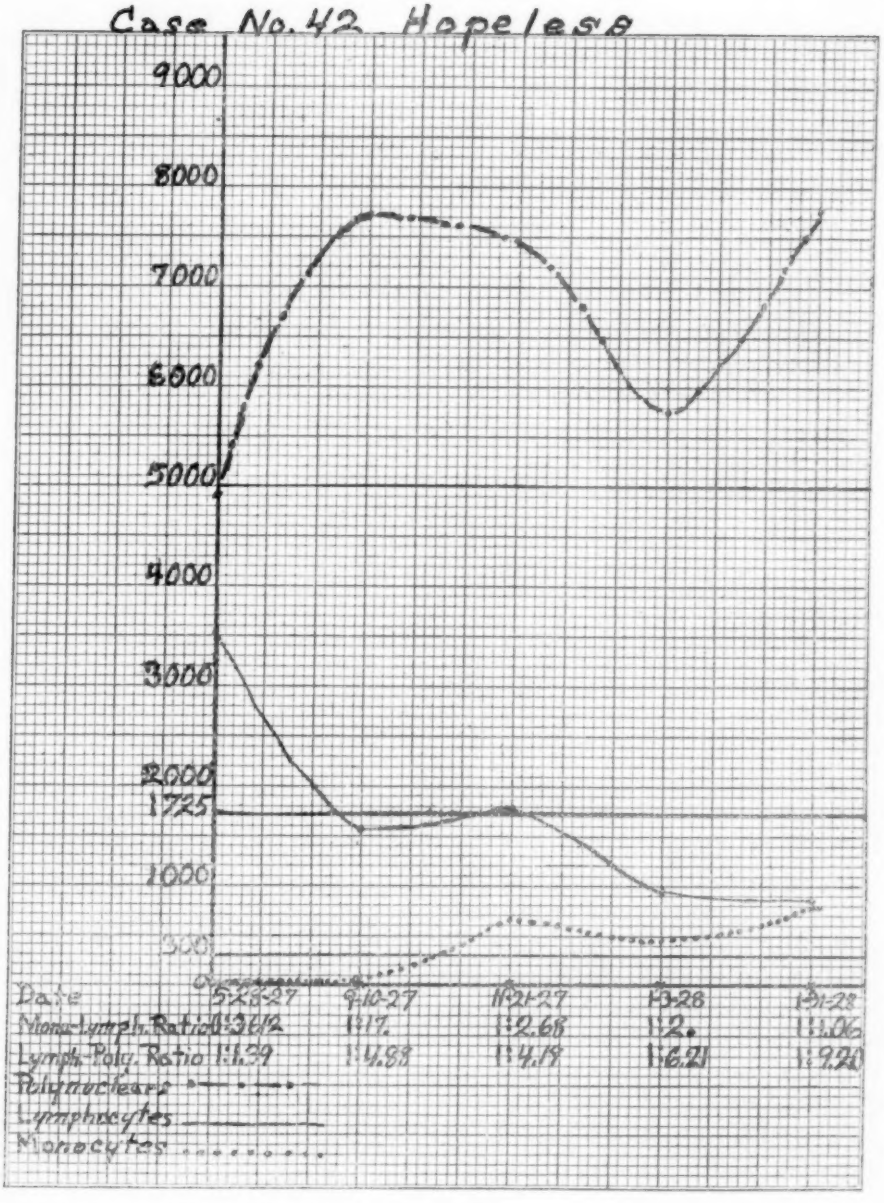

Case No. 42. Hopeless
9000
8000
7000
6000
5000
4000
3000
2000
1725
1000
500
Date
5-23-27
9-10-27
11-21-27
1-3-28
1-31-28
Mono-Lymph. Ratio 1:3.62
1:17.
1:2.68
1:2.
1:1.06
Lymph-Poly. Ratio 1:1.39
1:4.88
1:4.19
1:6.21
1:9.20
Polymorphears
Lymphocytes
Monocytes

CHART VII

definitely to an improved lung condition.

4. An increase in the percentages of neutrophiles and of monocytes, with a decrease in the percentage of lymphocytes points quite definitely to a more active and extensive lesion. The converse points quite definitely to an improved lung condition. Corresponding changes in the counts per cu. mm. of these cells point in corresponding directions, but less definitely.

5. This study tends to corroborate clinically the experimental work of Cunningham, Sabin et al, on the significance of the monocyte-lymphocyte ratio in the circulating blood of the tuberculous, and to confirm the conclusions of Medlar and his associates regarding the different parts played by the monocyte, the neutrophile and the lymphocyte in the histopathological reaction in tuberculosis.

The writer wishes to acknowledge with thanks his indebtedness to Mr. Theodore W. Keiper, A.B. in charge of the Pamsetgaaf Laboratory, and to Mr. Ernest Born, B.S. and Mr. O. P. Shook, Jr., for very valuable assistance in the technical and mechanical parts of this study.

Rheumatic Fever: Clinical Manifestations, Etiology, and Treatment*

By David Riesman, M.D., Sc.D., and James Craig Small, M.D., Sc.D.,
Philadelphia

WE DESIRE to discuss rheumatic fever under three aspects:

I. Clinical Manifestations.

II. Etiology.

III. Treatment.

1. The clinical manifestations subsumed under the name of rheumatism are exceedingly numerous. Wiesel (Med. Klin. 1923, xix, 163), found a total of eighty different pathological conditions included under the term rheumatism; we shall limit ourselves to ten, as follows:

1. Articular rheumatism or better acute rheumatic fever.
2. Some forms of tonsillitis and pharyngitis.
3. Chorea minor.
4. Cerebral rheumatism or rheumatic hyperpyrexia.
5. Certain types of heart disease.
6. Certain forms of muscular pains; growing pains in children; some forms of neuritis.
7. Various skin manifestations:
   a. Rheumatic nodules.
   b. Erythema multiforme.
   c. Rheumatic purpura (peliosis rheumatica.)
8. Certain forms of chronic arthritis, usually following recurrences of rheumatic arthritis.
9. Pleuritis.
10. Pneumonia.

There is evidence, in many instances purely circumstantial, upon the basis of which clinicians believe themselves justified in calling this heterogeneous group, rheumatic. But if to this group of seemingly diverse morbid conditions the term "rheumatic" is to be correctly applied, it can be done only on one condition—that they all prove to have the same etiology or that they all respond to the same specific treatment. Hitherto they have been placed together by nosographers solely on clinical grounds which it may be well to enumerate.

1. The less clearly defined conditions occur in persons who have had characteristic attacks of rheumatic fever. They are more or less influenced by atmospheric changes.

2. Tonsillitis is a frequent antecedent of rheumatic fever. In Swift's

*Read at the meeting of the American Association of Physicians in Washington, May 1928.

series this happened in about 50% of all cases.

3. There is a probable relationship between tonsillectomy and the cessation of recurrences in rheumatic fever.

4. Endopericarditis and myocarditis in children and in early adult life are rarely produced by anything else except rheumatic infection.

5. The fugitive myalgias and arthralgias of childhood often lead to disease of the heart identical with that produced by typical rheumatic arthritis.

6. The skin manifestations are found in persons who have shown other rheumatic manifestations.

7. Chorea occurs at about the same age period, interchanges with articular rheumatism, and leads to the same type of heart disease.

8. Some of the chronic arthritic changes are seemingly a connecting link between acute rheumatic fever and chronic arthritis—persistence of arthritic manifestations following acute exacerbations, the joints finally assuming the characteristics of rheumatoid arthritis.

It can readily be seen that the foregoing arguments are not of equal validity and that much more knowledge is necessary before a definite relationship can be established between the true disease rheumatic fever and some of the so-called rheumatic conditions.

As a result of clinical pathological studies, our conception of the nature of rheumatic fever has undergone a striking change. The disease hitherto considered an acute infection is now known to be often subacute and even chronic. The endocardial lesions though seemingly stationary are frequently not really quiescent, mild febrile periods with leukocytosis indicating a persistence of the infective process. Even in the absence of valvular involvement continuance of a rapid pulse and slight leukocytosis testify to incomplete recovery, the lesions in such cases persisting perhaps in the myocardium or in the endocardium in the form of the mural endocarditis described by McCallum. These significant facts have an important bearing on treatment, especially upon the length of stay in bed.

Earlier writers looked upon the cardiac involvement as a complication of rheumatic fever or as a sequela. But the frequency with which it can be demonstrated, (95% Swift, 61 out of 64, Rothchild, and in all out of 36 cases studied by Reid and Kenway, (New England Journal of Medicine, March 15, 1928); the fact that in children valvulitis may develop when joint manifestations are trivial, and the further fact that endocardial lesions sometimes precede the arthritic manifestations, led to the conclusion that the cardiac involvement is part and parcel of the rheumatic process and is no more a complication or a sequela than is involvement of the shoulder joint a day or two after that of the knee joint.

Rheumatic infections are on the decline in all parts of the world. This is shown in the figures prepared by the Surgeon General of the United States army and by Faulkner and White, (Journal of the American Medical Association, August 9, 1924.) These same authors show that hered-

ity is not an important factor in the spread of rheumatic fever; but that, as was demonstrated by St. Lawrence, (Journal of the American Medical Association, 79, 2051, December 16, 1922) contagion plays a rôle similar to that in tuberculosis. Grenet (Sem. des hôp. 3 :288, May, 1927) reports five distinct epidemics and there are records of multiple cases in the same household.

The influence of environment is also evident, the disease being distinctly rarer in children of the so-called better class of families. Among environmental influences must be mentioned climate. The potency of this is shown by Harrison and Levine, (Southern Medical Journal, December 1924) who found that rheumatism and rheumatic heart disease are much more common in Boston than in cities of the South.

The anatomic lesions of rheumatic fever deserve to be discussed as they throw light upon the clinical aspects of the disease. They are principally of two types: Proliferative and exudative. The latter are represented by the outpouring of serum into the joints and peri-articular tissues, pericardium and pleura; the former, by the so-called Aschoff bodies which most writers consider pathognomonic of rheumatic infection (not Friedrich von Müller, Am. J. Med. Sc., January, 1928).*

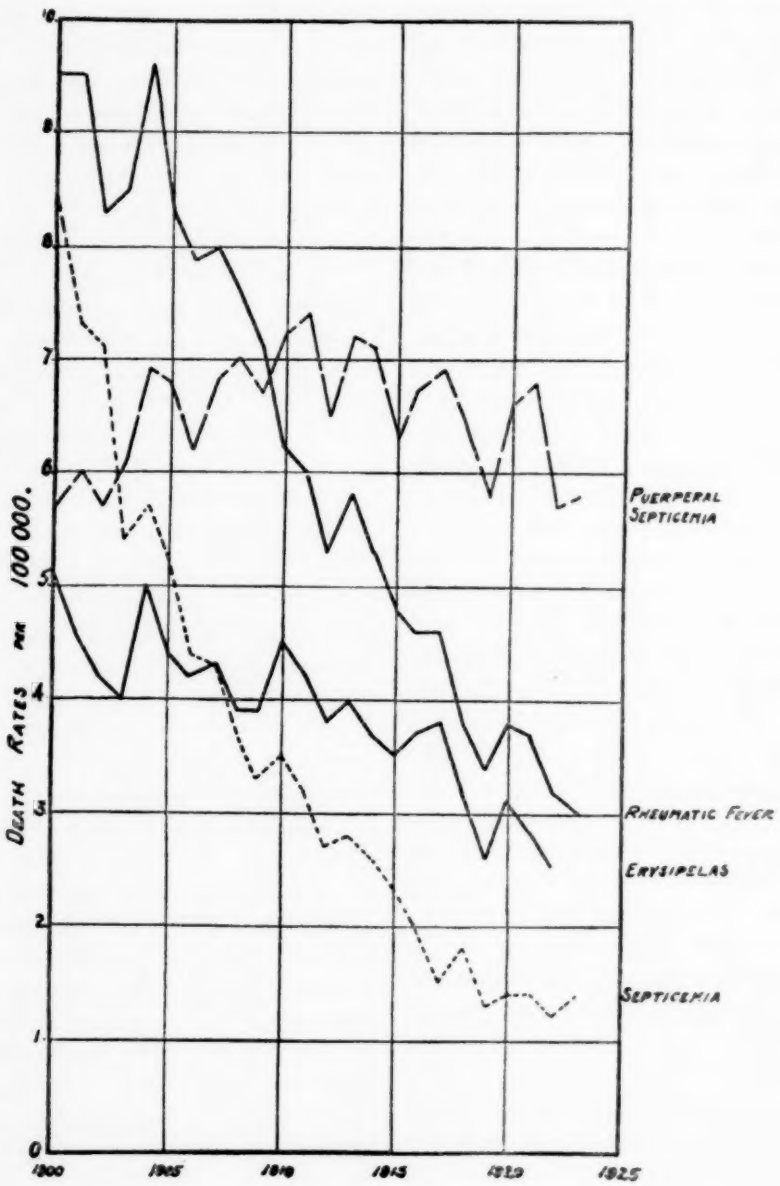
They consist of collections of cells mostly of irritation or giant cell type differing however from those of the tubercle. While these nodules are seen most characteristically in the heart muscle and in the rheumatic subcutaneous nodules they are also found in a modified form in the diseased valves, in the subserous layers of the inflamed pericardium, in the aorta (Pappenheimer and von Glahn, Journal of Medical Research, 1924, 44, 489), and in the brain in chorea. This last discovery, made by Poynton and Holmes, (Lancet, October 13, 1906, 982) at an early day is a strong argument in favor of the belief that chorea is due to an encephalitic rheumatic process which at times may be associated with meningitis. (Swift, Am. J. Med. Sc., November, 1924).

*They have recently been described in meningococcus infection (Rhoads, Am. J. Path., 1927, 3, 623).

Etiology

That rheumatic fever is an infectious disease cannot be doubted. There is even evidence, as already mentioned, of a certain mild contagiousness. Its seasonal prevalence corresponds to that of the acute respiratory infections. Frequently the disease is inaugurated by an attack of tonsillitis or pharyngitis. 'Atwater (see chart I) has recently shown (Am. Jour. Hygiene, May, 1927) that epidemiologically the incidence of rheumatic fever closely parallels that of the well-known streptococcus infections of scarlet fever, erysipelas, puerperal septicemia.

The association of a streptococcus with rheumatic fever was first observed by Poynton and Payne in 1900. Blood cultures in the acute attacks of rheumatic fever are sterile as a rule. In January, 1927, attention was directed by one of us (J. C. S.) to a streptococcus isolated from the blood of a typical case of rheumatic fever.


DEATH RATES PER 100 000.
0
1
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1925
PUERPERAL SEPTICEMIA
RHEUMATIC FEVER
ERYSIPELAS
SEPTICEMIA

Studies of this organism showed that it belonged to a distinct immunologic species. It was furthermore easy to isolate it from throat cultures of patients with rheumatic fever. It was also obtained from the cultures of the feces of some cases of chronic arthritis. The organism has been described under the name *Streptococcus cardioarthritidis,* (Small, J. C., Am. J. Med. Sc. 1927, 173, 101.) Further studies have shown its wide-spread distribution, the lesions produced by it in experimental animals, Belk, Jodziss, and Friedrick (Arch. Pathology, in press), and the appearance of immune bodies in the blood of patients with rheumatic fever, chorea, etc. The therapeutic application of antiserum, of vaccines, and of soluble products derived from the microorganism have also been investigated.

Strains of this streptococcus constitute the first compact serologic group found definitely associated with rheumatic fever (Kreidler, W. A., Jour. Infect. Dis., in press).

The organism is most readily obtained from throat cultures of patients with acute rheumatic fever and chorea. The mode of collecting material for such cultures is important. No attempt should be made to obtain material from the tonsillar crypts if the tonsils are intact. Material from the crypts ordinarily shows an abundant growth of streptococcus viridans, streptococcus haemolyticus and other bacteria. It is not the best source from which to obtain primary cultures of the streptococcus cardioarthritidis. The organism prefers the superficial sites in the pharynx—hence it is best to obtain the material on a sterile swab from the reddened streaks of the mucous membrane of the anterior pillars, uvula, or soft palate. We would make the suggestion that the peculiar superficial inflammation which constitutes the so-called rheumatic throat of the older clinicians may be dependent upon infection with this streptococcus. The throat that we have come to regard as associated with acute rheumatic fever and which yields the most abundant growth of the streptococcus in primary cultures might perhaps be described at this point.

The striking clinical feature in the throat in the acute phase of rheumatic fever appears in areas of intense redness of the mucous membrane of the anterior pharyngeal pillars on either side, which unite at the uvula, thus presenting an inverted crescent-shaped area of inflammation. In the most intense inflammatory reactions, this area spreads forward over the soft palate for a third to a half of its extent. Over the soft palate intensely congested small blood vessels stand out prominently. The inflammation appears to be very superficial. There is no tendency to ulceration, necrosis or the formation of an opaque exudate. Transparent mucus, in slight excess perhaps, may be collected upon swabbing such areas. The color of the inflamed mucous membrane is a very brilliant red during the acute stage; later as these areas recede the palate and uvula take on a bluish red color. The bluish red areas appear as vertical streaks on the anterior pillars and do not unite above to complete the crescent-shaped area. In the acute stages the brilliant red

inflammation may involve the pharyngeal mucous membrane generally. In the posterior pharynx, the lateral folds take on a deep red color, and are slightly thickened, presenting a velvety appearance. The nasopharynx also shows the intense redness.

The most reliable sign in the subacute cases is the definitely marginated red or bluish-red streaked areas on the anterior pharyngeal pillars, since here the contrast with normal mucous membrane causes the objective signs to stand out prominently in a location easily seen by the most casual observer. These red-streaked areas appear constantly in the throats of rheumatic fever patients regardless of whether the tonsils have been removed or not. We believe that in persistent rheumatic involvement the activity is directly correlated with easily observed signs of activity of the inflammatory reactions of the mucous membrane of the throat.

These observations suggest that the virus of rheumatic fever grows in certain superficial locations which are not removable by surgical means. The prevalent ideas of focal infection as a factor in the etiology of rheumatic fever may have to be modified to the extent that the focus will be regarded as not amenable to surgical treatment. The superficial character of the inflammation suggests also that the infection may spread over moist mucous surfaces, not only throughout the upper respiratory tract, but perhaps at times downward over the mucous membrane of the trachea and bronchi. A superficial mucous membrane involvement would also aid in an understanding of the rarity with which the virus gains access to the blood stream, and would add strength to the assumption that certain of the general manifestations of the disease are due to the absorption of toxic products of the virus, absorbed the more readily from the large surface of the mucous membrane involved in the primary infection.

In the present state of medical knowledge it is only possible to theorize in regard to the pathogenesis of the disease. From the clinical and pathological points of view, rheumatic fever as already mentioned appears to present lesions of two types—the exudative and the proliferative. That the causative factors responsible for these two types of lesions differ in certain basic particulars is a natural conclusion, especially as the symptoms produced by the former, the exudative lesions, appear so readily amenable to salicylates whereas those due to the latter, the proliferative, are wholly non-responsive to these drugs or are but slightly affected by salicylate acid medication.

It is not within the scope of this paper to discuss at length the hypotheses offered in explanation of the pathogenesis of rheumatic fever, but it is our belief that the dual nature of the lesions will eventually be accounted for by two sets of processes not entirely explained by any of the hypotheses advanced to date.

Treatment: We shall refrain from an historic summary—it is a long chapter of trial and error. The salicylates once held as specifics are no longer so considered although they have great value in the treatment of

certain phases of the disease. Nor will we dwell on the use of non-specific proteins since their very name indicates that they are not what science is looking for.

Menzer in 1902 reported favorable results from polyvalent antistreptococcic serum and looked upon the immediate febrile reaction as well as upon the later serum disease as factors influencing the results obtained.

For about 18 months antiserum (Rheumatic Fever, I & II, Small, J. C., Am. J. Med. Sc., 1928, 175, 638) prepared by immunizing horses with the *Streptococcus cardioarthritidis* has been in use and has been employed in the treatment of upwards of 270 patients in the Philadelphia General Hospital. For the past year special wards set aside for the study of rheumatic fever have aided greatly in the collection of observations upon which to base the present estimate of the efficacy of the treatment.

The serum was employed first in chorea and acute rheumatic fever, later also in certain forms of chronic arthritis in an effort to determine the relationship if any between these forms and acute rheumatic fever.

The antiserum has been prepared in horses and more recently in cattle—the two appear to be equally effective in treatment. The use of the bovine serum has been followed by very mild serum disease, hence it is preferable to equine serum which frequently calls forth a rather severe serum sickness. Since November 1927 a concentrated antiserum has been available. The amount to be injected is still empiric as so far no method has been developed for determining the relative antibody content of the different lots of serum. Experience has shown that the antisera now being produced are of such potency that the adequate dose ranges from 5 to 15 cc. Excessive amounts have not been followed by the definite alleviation of the joint symptoms or by that decline of temperature which had followed the use of smaller and seemingly adequate amounts. This paradoxical sequence of events following excessive doses has been attributed to focal inflammatory reactions arising at the sites of the union of antigen and antibody in such amounts as to give rise to a reaction similar to the Arthus phenomenon. In practice these focal reactions are prevented by avoiding the injection of excessive amounts of antibody and by administering the estimated adequate amounts of antibody in fractional doses, allowing from 12 to 18 hours to elapse between the injections of the several doses.

The focal reactions have not been noted in our limited observations upon private patients who were under full doses of salicylates at the time the serum was administered. Moreover focal reactions well established have responded to the administration of moderate doses of salicylates in from 18 to 24 hours.

A much more important phase of the treatment of the rheumatic diseases is concerned with the problem of active immunization. In general passive immunity conferred by an antiserum is of short duration, active immunity conferred by vaccines or by antigenic products of bacteria is of a

more lasting character. Rheumatic fever as a chronic continuing disease of the heart could scarcely be expected to respond adequately to serotherapy. We believe that relapses following serotherapy can be greatly reduced by the use of repeated injections of small amounts of vaccine or of the soluble products of *Streptococcus cardioarthritidis*. We have reason to believe that this combination constitutes an effective prophylactic therapeutic procedure in the rheumatic diseases.

The soluble antigen of *Streptococcus cardioarthritidis* in dilutions of 1:10,000 and 1:1,000 is the agent at present employed in attempts at active immunization. The 1:10,000 dilution is used in initial doses of not more than 0.5 cc. and maintained at this amount until no reaction following its injection can be detected. After that the doses are gradually increased by from 25 to 50% of the dose last given. The injections are administered subcutaneously and at intervals of from 5 to 7 days. The soluble antigen should be employed routinely in patients treated with antiserum. The injections may be started as early as the third day or may be delayed until after the period of serum disease has passed. In the subacute and chronic forms the antigen alone may be used.

The Dietetic Treatment of Diabetes Mellitus*†

A Restatement of the Fundamental Principles

By L. H. Newburgh, *Ann Arbor*

As long ago as 1914, F. M. Allen had demonstrated that the principle of undernutrition was vastly more successful in the reduction of diabetic hyperglycemia and glycosuria than the older methods in use at that time. Joslin enthusiastically adopted this principle and made it the central feature in the routine treatment of his diabetic patients. Both men emphasized the value of a sharp reduction of calories, but paid little attention to the source of the energy of the diet, with the exception that they permitted only minimal amounts of fat. Joslin felt it necessary to keep the fat as low as possible as a safeguard against acidosis and Allen in one of his publications stated that "fat is a poison for the diabetic."

In order to appreciate the great value of low calory diets it is necessary to recall to mind the composition of the diets in general use during the preceding era. From time immemorial it has been good practice to build up the body of the sick individual, and no exception was made in the case of the diabetic. In fact it was considered essential to add large increments to the weight of these patients, in order to counteract the emaciation so characteristic of that disease. In the second place every attempt was made to avoid carbohydrate. A typical diet of those days consisted of 200 grams of protein; 200 grams of fat, and a small amount of carbohydrate. The patient received some 2700 calories and very frequently continued to have a glycosuria. The therapeutic failure was attributed by Allen to excess of calories, but another and simpler explanation was brought to light by estimating the glucose value of the diet by Woodyatt's method. When this is done it is found that the sort of diet just described contains 150 grams, or more, of available glucose. Need we be surprised that all but the mildest diabetics continued to excrete sugar in the urine while living on such a diet.

If now the type of diet used by Allen and Joslin be analyzed in the same way, its great advantage is easily understood. Such a diet might have the following composition: Protein 50 grams; Fat 30 grams; Carbohydrate 50 grams; with a glucose value of only 80 grams. Most dia-

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†Presented to the Michigan State Medical Society at its annual meeting in Detroit, September 28.

betics are able to dispose of that amount of glucose.

But such a diet is intentionally deficient in calories. The prolonged and progressive undernutrition, with the accompanying incapacity caused by it, was accepted by its advocates as an unavoidable evil which was to be regarded as a welcome substitute for the distressing symptoms suffered by the uncontrolled diabetic.

In 1918 Marsh and I began an experiment designed to answer the question whether a middle course between these two extremes was not better than either of them. Our plan was to use a diet containing sufficient energy to maintain the individual following his usual occupation at a little less than the standard weight for his sex and age. In order to supply the two thousand to twenty-five hundred calories ordinarily required for low maintenance, and at the same time keep the glucose value of the diet low, it was necessary to use fat as the chief source of energy and to restrict the protein and carbohydrate because of their high glucose equivalents, as much as the principles of nutrition permitted. We had chiefly in mind that the diet should contain enough protein to establish nitrogen balance but no more, and that the total glucose of the diet must be great enough to insure complete combustion of the fat. Ladd and Palmer who determined the carbohydrate fat ratios when acetone bodies first appeared in the urine of diabetics, found that ketonuria did not occur until the fat of the diet was more than three times the glucose (calculated by adding 58 per cent of the protein to the carbohydrate).

A typical discharge diet used by us has the following composition: Protein 50, Fat 220, Carbohydrate 35. It has a glucose value[1] of 86 grams; a fatty acid,[2] glucose ratio of 2.6 and yields 2300 calories. In practice the patients were first desugarized by a diet of this type but much restricted in regard to energy. For this purpose we fed 15 grams of protein, 90 grams of fat and 12 grams of carbohydrate. The energy value is 960 calories. When the urine had been free of sugar for several days, proportionate increments were added to the diet until the desired maintenance level was reached or glycosuria reappeared. In the latter case the patient finally received a diet as near to his energy requirement as he could tolerate without glycosuria.

This procedure was used in the treatment of 190 consecutive, unselected cases. We then summarized our experience in the following terms: "a low protein, low carbohydrate, high fat diet produces and maintains an aglycosuric state, is not attended by acidosis and causes its disappearance when present (short of coma) at the beginning of treatment; maintains nitrogen balance; does not produce lipemia and causes its disappearance when present at entrance; supplies sufficient energy to avoid the evils of fasting and undernutrition and is not attended by downward progress in

[1]Total glucose = 100% of the carbohydrate + 58% of the protein + 10% of the fat.

[2]Fatty acid = 90% of the fat + 46% of the protein.

uncomplicated cases." This statement was published in 1923. The continued employment of the plan has merely strengthened our confidence in it.

It need scarcely be added that the administration of insulin, increases the responsibility of adhering strictly to proper dietetic principles. Everyone recognizes the life-saving quality of insulin in the treatment of diabetic coma. On the other hand, in the routine treatment of the controlled diabetic it should only be used to aid the patient in obtaining sufficient energy for maintenance when a diet containing his caloric requirement causes glycosuria. This conclusion is based on the conviction that insulin increases quantitatively the total amount of internal secretion but is in no sense curative. If the physician will employ the kind of diet described above he will find that four fifths of his adult patients do not need insulin. In the case of children, because of their much greater caloric requirement, insulin is necessary to promote normal growth in most of these patients. During the past year we prescribed diets for 347 diabetic patients. Two hundred and fifty six of them, or 74% were able to take a maintenance diet of 2200 calories or more, without insulin. The total glucose of the diet was at least 90 grams.

It needs to be emphasized that the low protein, low carbohydrate, high fat, maintenance diet, is the inevitable result of the application of the laws of nutrition to the special metabolic problem of the diabetic. With this simple fact in mind, we can not avoid regarding Joslin's (1) recent adverse criticism of this dietetic procedure as an unjustifiable interference with a method that is working well. He finds that 47% of his 609 diabetic deaths since the introduction of insulin were due to disease of the arteries (we refrain from questioning how many of these diagnoses were confirmed by autopsy, and how much this incidence of arterial disease exceeds that of a similar age group from the general population).

According to Joslin the prevention of arteriosclerosis is favored by reduction of weight to the normal level. Advice that we heartily accept. But we are incapable of finding any sound basis for the statements that: "The avoidance of a high fat, low carbohydrate diet is another preventive influence. I suspect that the development of arteriosclerosis in our diabetics has been caused largely because the carbohydrate in the diet was lowered and the fat increased out of all proportion. Prior to weighed diets this resulted in coma but with undernutrition and insulin, patients avoid coma and live long enough to show the more subtle effect of the high fat diet, namely atheromatosis." To support these sweeping statements Joslin refers to the record of a patient reported by a colleague. This mild diabetic who died at the age of fifty-eight had lived on a diet "low in carbohydrate with an excess of fat." During the last five years of his life his weight rose from 97½ pounds to 174 pounds. The autopsy disclosed severe vascular disease throughout the body. Can Joslin, who has taught all of us the importance of keeping down the body weight of the

diabetic, seriously expect us to believe that this patient who gained 76½ pounds in five years became arteriosclerotic because the fat in his diet irritated his blood vessels. Would the great advocate of undernutrition have us forget that the glaring fault in this patient's diet was its excess of calories?

It is unfortunate that Joslin's paper does not contain a tabulation of the level of blood fats of patients alleged to be harmed by an excess of fat in the diet; for it is well known that the untreated or improperly treated diabetic often shows a marked lipemia; and all agree that its decline is excellent evidence that a proper diet has been prescribed.

Some years ago Marsh (2) and Waller showed that diabetic lipemia was rapidly reduced by the high fat diets used in this clinic. In their summary they wrote, "It is certainly very strong evidence that the prevalent assumption which postulates that diabetic hyperlipoidemia is dependent on the excessive ingestion of fat is unwarranted." A summary of some of their data is reproduced in Table 1.

TABLE 1

Total Blood Lipids		Interval
Before Treatment	After Treatment	Days
Gms. Per Cent	Gms. Per Cent	
1.59	1.54	20
2.73	1.10	38
8.1	2.09	66
3.31	1.01	260
2.63	1.00	395

Recent studies (3) at the University Hospital have beautifully shown that the lipemia present in a group of patients was dependent upon the calories of the diet and that it was uninfluenced by the dietary fat.

The important facts taken from the record of one such patient will serve as an example. A young man who had been moderately obese for many years came to the hospital for the treatment of xanthomata. While still on an uncontrolled diet two determinations of his blood lipids gave the following readings: Total lipids 2.275 and 2.215 grams per cent; and cholesterol 0.323 and 0.316 grams per cent. The serum was creamy in appearance. Further examination showed that he was diabetic. He was desugarized and then given a series of diets containing increasing amounts of carbohydrate. During this period of thirty-five days he lost twenty-nine pounds due to the low energy values of the diets. The xanthomata began to involute shortly after the diabetic diets were begun and had disappeared before the end of this first period. Throughout the second period of thirty days his diet consisted of protein 55 grams, fat 210 grams and carbohydrate 300 grams. These 3310 calories daily caused a gain of eight pounds and a return of the xanthomata and the glycosuria. The blood fats at the end of this second period were: Total lipids 2.416 grams per cent and cholesterol 0.400 grams per cent. Finally he was given a diet containing the same amount of protein and of fat but only 100 instead of 300 grams of carbohydrate. It yielded 2510 calories. The patient again became sugar free and the xanthomata began to disappear. He

neither gained nor lost weight. After forty-five days on this diet, the blood fats were as follows: Total lipids 1.175 grams per hundred and cholesterol 0.225 grams per hundred. The important figures for our present purpose are brought together in Table 2. The table makes it clear that the marked lipemia which resulted from a high fat diet excessive in calories, was reduced to half its former value in forty-five days by a second diet containing the same amount of fat but whose calories had been lowered to the maintenance level. It is evident that, in this patient, fat was without effect upon the lipemia except in so far as it was a source of calories.

TABLE 2—THE RELATION BETWEEN CALORIES AND BLOOD FATS

Diet				Blood Fats		
Protein	Fat	Carbohydrate	Calories	Total Lipids	Cholesterol	Remarks
				Mgs. Per Cent	Mgs. Per Cent	Gain of 8 pounds in 30 days
55	210	300	3310	2416	400	Glycosuria
55	210	100	2510	1175	225	Weight constant Urine normal

CONCLUSIONS

Some clinicians believe that diabetic arteriosclerosis bears a casual relationship to the patient's diet. At present there is insufficient evidence to either prove or disprove this hypothesis.

If such a relationship exists, the fault lies in excess of calories. The vascular disease is not caused by the metabolic products of fat and the latter may take part in the production of arteriosclerosis only in so far as it is a source of calories.

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Some of the Difficulties in the Diagnosis of Cancer of the Internal Organs*

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IN 1927, 14,254 people died of cancer in the State of New York. Of these deaths, 7,448 or 52.2 per cent occurred in the City of New York, and 6,806 or 47.8 per cent occurred in the remainder of the State. There were 4,790 cases of death from cancer of the stomach and liver, or 33.6 per cent of all the deaths from cancer. Of these deaths 2,547 occurred in New York City, or 53.1 per cent, and 2,243 occurred in the remainder of the state, 46.9 per cent. There were 2,404 deaths from cancer of the peritoneum, intestines and rectum, or 16.8 per cent of all the cancer deaths. Of these 1,256 deaths, or 52.2 per cent occurred in the City of New York, and 1,148 deaths or 47.8 per cent occurred in the remainder of the State. These figures represent crude death rates and were taken from the Vital Statistics Review of the New York State Department of Health, 1928, xiii:214.

It will be noted that the percentages of deaths from cancer of all parts of the body and from cancer of the digestive tract in New York City and in the State outside of New York City, are almost identical.

In its attack on the cancer problem, the American Society for the Control of Cancer has adopted the slogan, "In Early Treatment Lies the Hope of Cure." Early treatment cannot be undertaken unless early diagnosis is made. Cancer of the various parts of the digestive tract and other internal organs is not easy to diagnosticate in its early stages. The object of this paper is to point out some of the difficulties in early diagnosis. It is sometimes necessary, especially for a consultant, to give an opinion concerning a specific case of disease without time to accumulate the information obtainable by the employment of recently developed diagnostic methods dependent upon the use of chemical and physical technique.

In 1913 I saw a man, aged sixty years, who complained of having lost fourteen pounds in weight within two months. At the age of thirty-seven he had had an attack of typhoid fever which lasted altogether about three months. For the two months before the time he was first seen, he had been sleeping poorly. He had no other symptoms except some slight

*Read at a meeting of the Staff of the Park Avenue Hospital, Rochester, January 11, 1928.

morning expectoration. Glucose had been found in his urine at some previous time and he had a chronic nasopharyngitis. The man was a hearty eater and apparently ate more carbohydrate than proteid food. Upon physical examination it was found that he had a moderate amount of pulmonary emphysema, a slightly increased area of cardiac dulness (oblique diameter 17 cm.) a weak heart muscle, a palpable liver edge, and a low blood pressure (systolic 109 mm.). He was then twelve pounds over weight and there was a trace of glucose in the urine. During the following ten months, he lost eighteen pounds more so that he was about six pounds under weight. He was not, however, complaining of symptoms, and had reported for physical examination only. The liver edge was palpable on deep inspiration but there were no areas of tenderness in the abdomen. In the following years he had frequent attacks of general muscular pain, fever and constipation, with occasional other manifestations like herpes labialis and glycosuria. During this period his weight fluctuated so that at one time he had gained twenty-one pounds over his lowest weight. He was thought to be a man having a chronic nasopharyngitis with periodic exacerbations, and possibly a subacute cholecystitis. In September, 1917, he began to complain of his usual symptoms with the addition of a good deal of abdominal pain, which he ascribed to eating corn. He also said he was "low spirited and felt mean." He was seen at 8 P. M. when he acted as though he had been drinking, his temperature was 99 degrees, pulse 100, respirations 24. The tongue was coated, the abdomen was distended, there was epigastric tenderness and the liver edge was palpable. He was thought to be undergoing one of his usual attacks of acute exacerbation of his chronic nasopharyngeal disease with an added digestive disturbance. He did not do well and a surgeon who saw him thought he had carcinoma. He was operated upon and a diffuse inflammatory condition involving the surface of the liver with omental adhesions overlying a carcinoma of the liver was found. The primary source was unknown. The rectum was negative. the stools showed no occult blood and the X-ray pictures suggested no lesion in the stomach or the bowel. He died a few days after the operation. No autopsy was allowed.

The question arises whether this patient, when first seen in 1913, having lost fourteen pounds in weight, having a history of glycosuria, and a palpable liver edge had a beginning carcinoma, perhaps of the pancreas. If so the periodic attacks of fever, general muscular pain and constipation that he had during the four following years might be due to the extension of the growth and not to acute exacerbations of a chronic nasopharyngitis. If so, would operation at that time have resulted in complete removal of the growth and cure? The finding of malignant disease of the liver in the 1917 attack was a complete surprise to me. The attack seemed in no way to differ from previous attacks, except for the suggestion of alcoholic intoxication on the first evening of its development.

If we are to prevent cancer of the liver and pancreas, we must look for a way to decide whether to operate when the indications are as indefinite as loss of weight, glycosuria and a palpable liver edge. Very likely a history of typhoid fever, followed by a palpable liver edge, occasional glycosuria, and sharp loss of weight ought to warrant a search for a beginning carcinoma. At all events we ought to keep constantly in mind the probability that all individuals beyond the age of forty-five may have beginning carcinoma.

In October, 1913, I saw a man aged forty-nine years who had complained of somnolence for almost eighteen months. Later he began to get yellow, and complained of pain at the costal border as though his "liver were a piece of wood pressing his ribs." In the previous five or six years he had lost some weight, but during the years just past, he had gained a little. He complained of chilly sensations all the time. When he would bend his body to the right he felt as though there were something hard in his abdomen. His appetite was not good. On physical examination he was found to be slightly jaundiced, there were numerous purpuric spots on the skin of the arms and trunk. In the standing posture the abdomen was prominent, but when the recumbent posture was assumed the prominence disappeared. The lower border of liver dulness was obtained at 6.5 cm. above the umbilicus. The liver edge was distinctly palpable, hard and painless, except a little to the right of the midclavicular line, about 5 cm. above the umbilicus, where fairly firm and deep pressure brought out pain. The spleen edge was indistinctly palpable and slightly tender. The stomach tympany extended from the sixth rib to the eighth rib. The greater curvature of the stomach was 4 cm. above the umbilicus. There was a moderate amount of cyanosis in the recumbent posture. A blood count gave the following results: Erythrocytes, 4,460,000; leukocytes, 8,880; hemoglobin, 89% (Sahli); color index, 0.99. Differential count: polymorphonuclear neutrophiles, 70.0% = 6,216; lymphocytes, 22.9%; large mononuclears, 4.8%; eosinophiles, 2.4%.

The following is an abstract of the opinion which I wrote to the physician who referred the patient to me: I have a feeling that you had better operate on this patient. I am inclined to believe you will find chronic infection of the bile passages. Of course, the case is not typical. The following features seem to me to point to cholecystitis: The presence of chilly sensations all the time, the variation in the jaundice, the amount of bile in the stools, the blood count, which, while it does not show a leukocytosis, does show a fairly high polymorphonuclear percentage. I think you can definitely exclude cancer for although the patient is twenty-six pounds under his highest weight, you assure me that he has remained stationary or gained a little during this illness. Furthermore, according to Da Costa, cancer of the liver has a most constant and a most striking leukocytosis (Clinical Hematology, 2 ed. 1907: 476). I believe if the disease were malignant there would be a more

pronounced anemia. Twelve days after this opinion was written, the patient had an attack of abdominal pain and diarrhea, with fever to 103 degrees and localized tenderness in the gall bladder region. Two days later the man was operated upon. There was a moderate amount of ascites, the liver was nodular and hard. The gall bladder was enlarged and was bound down beneath the liver well over to the right side; its surface was nodular. There were two hard nodules in the head of the pancreas. The histological examination has been lost. The operating surgeon felt sure that the disease was malignant.

A man, aged forty-eight years, complained of regurgitation of food and vomiting. He had had stomach trouble for ten years. He began by regurgitating his food; at first the material was not sour but later it became sour. About six years later he began to complain of nausea but at that time there was no vomiting. About six months before he was first seen he began to vomit, at first the vomitus was watery but later it contained food, very little changed in appearance. At first the attacks of vomiting were not frequent, but during the last month or two he had vomited more frequently; sometimes every day, sometimes two or three times a week. He had not vomited blood. He complained of distress and griping pain in the stomach, gas and borborygmus. Sometimes he had diarrhea. He had an attack with fever about a month before I saw him in which his bowels moved every hour, the stools, which were greenish black in color, contained mucus, but no blood. There was a bad taste in the mouth, gas in the stomach and intestines, and often sharp cramps in the thighs and the legs at night. His appetite was entirely lost. He thought he had lost twenty pounds in weight in the previous month. On physical examination extensive dental caries with recession of the gums was found.

The following is an abstract of the abdominal examination: "The abdomen measures 69.5 cm. in circumference. The abdomen is retracted. There is a distinct pulsation in the line of the abdominal aorta. The left side of the upper segment seems a little fuller than the right. The inguinal lymphnodes are palpable on both sides. There is some tenderness on deep pressure in the left upper quadrant. There are no tumors. In the midline 2.5 cm. above the umbilicus there is a distinct area of tenderness. Stomach: The stomach tympany measures 21 x 12.5 cm. In the left midclavicular line the stomach tympany extends from the sixth interspace to 4 cm. below the costal margin. The greater curvature of the stomach is at the umbilicus. Examination of the pyloric end of the stomach for tumor is negative. After inflation the stomach tympany measures 23.5 x 14.5 cm. In the left midclavicular line the stomach tympany extends from the sixth rib to 4 cm. below the costal margin. The greater curvature of the stomach is 1.5 cm. below the umbilicus. There is a good deal of borborygmus. The patient complains of a sensation of smarting and burning and while the gas was in his stomach he vomited a moderate quantity of white frothy material."

I gave the following opinion: "I believe the case to be one of simple dilation of the stomach. You will see by the record that I inflated his stomach and determined a considerable amount of dilation with a greater curvature well below the umbilicus. I do not believe the dilation is dependent upon pyloric obstruction. I doubt very much if there is an ulcer, although, of course, the possibility of an ulcer of the duodenum must be kept in mind." I did not think the case was one of cancer of the stomach. Four days later gastrectomy was done and the pyloric third of the stomach was removed. There was a round mass as large as a golf ball connected with greater curvature of the stomach presenting ventrally. The wall of the stomach was thickened. There were numerous enlarged lymph-nodes along both the greater and the lesser curvatures of the stomach. On opening the removed portion of the stomach an infiltrating mass was seen involving the entire wall of the organ, resembling enlarged rugae. This mass extended all the way up to the removed portion. There was no ulceration. The pylorus was patent. Upon incision the rounded mass, already described in relation with the greater curvature of the stomach, was found to be filled with broken down, granular and fluid material resembling the contents of a tuberculous lymph-node. Histologic examination showed the growth to be a scirrhous adeno-carcinoma of the stomach. The patient died two days after the operation.

At the time of my study of the case, I was so sure that it was one of simple gastrectasis from improper dietary habits complicated by mouth infection that I did not suggest an X-ray examination. The possibility of carcinoma was evidently considered, as indicated by the note about tumor. The man went from me to the surgeon who operated on him who felt that there was a mass in the stomach region and recommended X-ray examination, which demonstrated the mass. The case illustrates the importance of keeping the possibility of carcinoma in mind in spite of a symptomatology which is not characteristic of malignant disease. It should be pointed out that this patient showed no evidence of gastric bleeding and that no mass was felt. Nevertheless, we must always be suspicious of carcinoma in cases of persistent indigestion. If we wait for the classical symptom complex, indigestion, loss of weight, anemia, and tumor, we shall be too late to accomplish cure by any method whatever. In any case of persistent indigestion X-ray study of the gastro-intestinal tract is demanded, particularly a fluoroscopic study.

A woman, aged fifty-four years, married, complained of pain in the right leg of five months duration. The pain began after an attack of an acute respiratory infection of the laryngeal type, which had lasted about five weeks. The pain was dull, and radiated to the right knee and to the back. She complained of being easily tired; had lost twelve pounds in weight in five months; and said that she had a tendency to pass urine involuntarily on coughing. Owing to the fact that she had never been pregnant; that the physical examination

was negative; and that there was pus in the urine I sent her for a pelvic examination. This showed a "Fibroid tumor the size of a grape fruit causing pressure symptoms of the bladder." The gynecologist recommended hysterectomy but the patient did not wish to follow the advice and, since she had passed the menopause, I did not urge her to have operative interference. Five months later she was seen again, complaining of pain low down in the back and soreness on the anterior surfaces of the thighs. She also complained of gas in the stomach and on six occasions she had vomited about five hours after her supper. The vomitus consisted of mucus and undigested food. There was no hematemesis and no coffee ground vomiting. She had lost no more weight but now I could determine, on examination of the abdomen, that it was uniformly distended, with tenderness in the right lower quadrant and in the epiagastrium. There was a small, hard tumor in the hypogastric region; deep down. In the right upper quadrant to the right of the median line and above the umbilicus there was a mass, hard, not tender. On deep respiration the lower border of the liver seemed to cover it. I ordered a cathartic for the patient and asked her to bring me a twenty-four hour specimen of urine. After taking a part of the cathartic ordered she vomited about a quart of mucus with a good deal of retching. The vomitus did not contain blood and did not resemble coffee grounds. The patient brought 20 c.c. of urine which she said was her entire twenty-four hour output. I thought that the fibroid tumor had become jammed in the pelvic inlet; that the mass in the right lumbar region was a hydronephrosis, and that the vomiting was due to an attempt on the part of the gastric mucosa to excrete urea. The surgical consultant thought the disease was malignant and that the mass in the lumbar region was a metastatic growth. At operation a "large malignant tumor filling the pelvis, fixed about the pelvic brim, involving by direct extension both ureters (was found). Retroperitoneal metastases were present especially in right side chain. Mass discovered in right upper quadrant is large metastasis matted in region of right kidney." The patient died several days after the operation of suppression of urine. No autopsy was allowed.

The question of uterine myomata is one of major importance and it is a question upon which the internist is frequently obliged to express an opinion. It seems to me that the advice of Crossen is the most conservative and offers the best prospect for prolonged life and freedom from illness for the patient: "A myoma of the uterus which has reached a size to be appreciated clinically is a more serious affection than is generally supposed. A considerable proportion of patients develop fatal local conditions; another considerable proportion of the patients develop serious visceral degenerations, and a large proportion finally pass into a condition of chronic suffering and invalidism." (Diseases of Women. Ed. vi:596.)

In June, 1914, I saw a woman aged sixty-three years. In October, 1912, her left breast had been amputated

for carcinoma. In January, 1914, she began to complain of dyspnea. The dyspnea was constant, but was made worse by excitement and by exertion. Recently she had become quite nervous. In March an area of flatness was discovered at the base of the right chest which was thought to be due to pleural effusion, but no fluid was obtained on tapping. Three weeks before she was first seen the dyspnea became worse and she began to notice palpitation, slight cough and some expectoration; no hemoptysis. She had lost between ten and twenty pounds in weight. On physical examination numerous hard, rounded painless nodules were found in the scar of the breast amputation, some of which were attached to the underlying tissues. The left axillary lymphnodes were enlarged, hard and adherent. Bronchial type of breathing was heard over the anterior portion of the left lung and in the left axilla and a few scattered adventitious sounds were heard, which did not clear up on coughing. Posteriorly, over the left lung the breath sounds were of the tubular type and adventitious sounds were heard similar to those heard anteriorly. Over the right lung, anteriorly, posteriorly, and laterally the breath sounds were slightly exaggerated and the expiration was somewhat prolonged, occasional adventitious sounds were heard, which were not cleared up on coughing. The liver edge was palpable, but not tender. The area of cardiac dulness was a little increased (oblique diameter 16 cm.). There was a soft systolic murmur in the second left interspace not transmitted. The pulse was 86, arteries distinctly palpable, thickened and somewhat beaded. The systolic blood pressure was 210 mm. (Tycos). The urine contained albumin, pus, several epithelial and hyaline casts. In view of the increased heart size, atherosclerosis, hypertension, albuminuria and casts. I thought the pulmonary signs, the dyspnea and the cyanosis were the result of the nephritis. In the opinion written to her physician I said "The carcinoma is undoubtedly recurring in the scar of the (breast) amputation and in the left axillary lymphnodes. There is a definite dry pleurisy, whether this is due to the nephritis, which is possible, or to the extension of the carcinoma to the pleura is a difficult question to decide. There is no definite evidence of the existence of an effusion in the right pleural cavity except the pleural frictions that are to be heard in that region."

Four months later I saw the patient again. For awhile after the first consultation she had done well. But the dyspnea had returned just before I saw her. There was no chest pain but there was some cough and an expectoration of a moderate amount of white mucus which was sometimes blood tinged. The physical examination on this occasion showed contracted pupils, a bulging at the lower left costal border, consolidation of the lower lobe of the left lung, and of the lower lobe of the right lung, with compensatory emphysema of the remainder of the lungs, no adventitious sounds were heard. I wrote the following, "Impression: owing to the history of previous carcinoma of the breast and the occurrence of a

nodule in the scar over the right deltoid muscle, I feel that the consolidation at the base of the left lung is due to extension of the carcinoma to the lung, although I think it curious that there is no more pain. The physical signs at the base of the right lung I take to be the result of old pleurisy; but it may be carcinomatous. The emphysema at the apices of the lungs is compensatory. On account of the high blood pressure, the contracted pupils and the occurrence of albumin and casts in the urine, it is just possible that the whole pulmonary complex is the result of nephritis."

The patient died five days later. An autopsy was obtained which, among other things, proved that the pulmonary symptoms and signs were due to the carcinoma of the pleura, carcinoma of both lungs (bases) and pulmonary emphysema (upper lobes). The kidneys were the seat of a chronic parenchymatous nephritis. There were 500 cc. of blood-stained fluid in the left pleural cavity.

The Symptoms of Dissecting Aneurysm of the Aorta*

By Leslie T. Gager, M.D., *Washington, D. C.*

DISSECTING aneurysm of the aorta presents a clinical paradox: the anatomical changes which are thus produced are easily among the most striking lesions of the circulatory system, and yet the diagnosis has been made during life only with the utmost rarity.

Interesting myself in the subject after my own failure to recognize an outspoken example, a survey of the literature, from Morgagni (1) to the present year, discloses a total of 382 case reports of dissecting aortic aneurysm, with mention, but not the data, of at least 30 additional cases. Dissections within the heart, or those confined to the smaller arteries are not here included.

In this whole series, it appears that the diagnosis of dissecting aneurysm was made in five instances—the patients of Swaine (2), Wyss (3), Mager (4), Davy and Gates (5), and Moosberger (6). The presence of the aneurysm, but not its type, had been recognized by Finny (7) and in the case of the patient mentioned by Osler (8), 30 years before the man's death.

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It becomes of interest, then, to inquire what symptoms and signs are produced by dissecting aneurysm of the aorta that might lead to its more frequent diagnosis. This problem gains practical importance when it is found that no inconsiderable number of these patients may go on to recovery, and that certain others, under errors in diagnosis, have been subjected to surgical operation. I am convinced that pathognomonic features do occur. To appreciate the symptomatology, the underlying pathological changes must be borne in mind.

Definition and Pathophysiology

The formation of a dissecting aneurysm begins with a rupture, usually a lineal tear, in the intima of the aorta. The second stage is that of the dissection of the layers of the media lengthwise and around the vessel. The extravasating blood takes the path of least resistance, for the connective tissue binding together the layers of the media is more easily torn asunder than are the elastic fibres of which these layers are composed. The stage of perforation is reached when the advance of the dissecting column of blood is in any way obstructed. In most instances this rup-

ture occurs externally, through the adventitia, and since by reason of hemodynamic stress and anatomical structure, the majority of dissecting aneurysms involve the first portion of the aorta, hemorrhage into the pericardium is by far the most frequent terminal event.

In approximately one case out of six there occurs the remarkable phenomenon of rupture of the new channel internally, into the lumen of the aorta, so that the blood from the false passage regains its normal pathway. In this event, the walls of the dissected area become lined with a new intima, may be further strengthened by connective tissue proliferation, and the result is a "healed dissecting aneurysm (9)." In consequence, the patient may live, even without consciousness of a circulatory defect, for many years.

Dissecting aneurysm, in short, forms a "tube within a tube," which may extend the length of the aorta and involve the whole or part of its circumference. In the process of dissection, the arterial trunks springing from the aorta may be compressed or occluded, and not uncommonly the smaller arteries, such as the intercostals, are entirely torn away from their sites of origin.

Etiology

Arteriosclerosis furnishes the common substratum for the primary intimal rupture, the immediate cause being sudden physical strain, trauma, excitement, all factors which induce circulatory stress. And it is not the grossly calcified plaque, but the "hyaline fibroid" lesion of Adami (10), at once brittle and closely connected with the media, which is peculiarly involved. Therefore, while dissecting aneurysm is largely a lesion of later adult life, it is a commentary on the development of aortic atheromata that many ruptures have occurred in the fourth, and even at the end of the third, decades.

Infectious processes involving the aortic tunics undoubtedly play a rôle in younger people, but syphilis, it is important to note, is a relatively insignificant factor. Thus von Schnurbein (11), in 91 carefully analyzed cases, found only one instance of definite syphilitic involvement and Loeschke's (12) small series of cases is only an exception to the general rule. The best explanation is that the characteristic syphilitic mesaortitis disrupts the orderly arrangement of the layers, and makes for local sacculation rather than wide dissection.

In young adults and children, there is an interesting group where coarctation, or stenosis, of the aorta is the factor which leads to dilatation and rupture of the first portion of the aorta.

In some instances, the anatomic changes in the aorta are slight or absent.

Clinical Classification

On the basis of their clinical features and course, it is possible to divide patients with dissecting aneurysm of the aorta into three groups:

1. Those in whom the rupture of the intima, dissection of the media, and perforation of the adventitia take place within a few seconds or min-

utes, and death is sudden and without previous warning.

2. Those in whom the process goes on more slowly, the stages are separated by varying intervals of time, and symptoms and signs of disease arise which are susceptible of observation, analysis, and diagnosis. In this group, the intimal tear may cause pain and collapse, a period of freedom from symptoms may ensue, and then some element of strain brings about the terminal phenomena, days, weeks, or months after the prodromata.

3. The group of those in whom the dissected channel reenters the normal passage, and "healing" takes place. Obliteration of the false passage by thrombosis and replacement fibrosis is rare.

In these patients life is indefinitely extended, sometimes with, and often without, symptoms of circulatory disease. In the end, these persons die of other causes, and only occasionally of delayed aneurysmal rupture.

In the second and third groups, therefore, one may consider the possibility of a syndrome which will suggest or establish the diagnosis of dissecting aneurysm, differentiate it from confusing conditions, and perhaps permit the institution of measures which will increase the number of those in whom "healing" takes place.

Symptomatology

The anatomic and physiologic considerations suggest that dissecting aneurysm of the aorta can produce a bewildering variety of clinical phenomena, and bedside experience proves this to be true. But certain predominant features appearing in numbers of carefully observed patients result in a reasonably characteristic picture, as may be made clear by a few briefly presented case reports.

Case 1 (13).—A man, aged 37 years, stout and plethoric, previously well, in the middle of a heavy meal, fainted. On recovery, he complained of violent abdominal pain and nausea, with pain in the back. The pulse was feeble and irregular, and the abdomen swollen and tense, but not very tender.

Next day, there was severe pain in the loins, radiating to the testicles. The pulse was now full. Clear urine was passed.

On the third and fourth days, there were suppression of urine, drowsiness, twitching, and the appearance of complete left-sided hemiplegia. The right radial pulse was smaller and feebler than the left, but the right common carotid pulsation was markedly increased over that of its fellow. At the base of the heart and over the innominate artery was heard a rumbling bellows murmur.

Passing through a period of great weakness, the patient was gradually improving, when, on the eleventh day of illness, being raised in bed for a drink, he fell back dead.

A dissecting aneurysm was found extending from just above the valves to the renal arteries. Rupture was into the pericardium. The dissection involved the innominate and right common carotid, the lumen of the latter being obliterated by the external compression. The right side of the brain was anemic, with softening in the area supplied by the middle cerebral artery.

Case 2 (14).—A man, aged 68 years, of spare habit and abstemious life, had chronic hypertension, cardiac enlargement to the left, dilatation of the aorta, and a basal diastolic murmur. There was moderate sclerosis of peripheral and retinal arteries. The Wassermann and Kahn blood tests were negative, and there was no evidence of syphilis.

Three weeks after a short attack of oppression in the upper chest, lasting an

hour, the patient was seized, two hours after eating a rather full meal, with intense pain beneath the upper sternum, radiating down the outer side of the left arm, and followed, within an hour, by pain in the lower lumbar region of the same constancy and intensity.

Both the substernal and lumbar pain persisted during four days, gradually subsiding and disappearing on the fifth day. The blood pressure remained high, was equal on the two sides, there were no notable changes in heart signs, the urine remained clear, there was a slight febrile movement.

The pulse became irregular and an electrocardiogram showed periods of sinoauricular block and numerous nodal premature beats, but no evidence of coronary artery thrombosis.

Death occurred suddenly on the seventh day, after the appearance of Cheyne-Stokes respiration and a terminal rise of blood pressure to 230/160 mm.

There was a dissecting aneurysm extending from the arch to the bifurcation of the aorta, with perforation into the mediastinum and left pleural cavity. The dissected channel was lined in part with a smooth intima. The aortic cusps were normal, there was moderate atheromatous change in the aorta.

Case 3 (15).—A man, aged 38 years, uncommonly strong and well developed, with the effort of reining in two "green" horses, suddenly felt a sharp, sticking pain in the breast, with headache and nausea immediately following. From this attack he recovered promptly, but next day his horses shied, and it took all his strength to control them. Now with greater intensity occurred the pain in the chest, with vomiting, weakness, and loss of power to see or speak for 12 hours.

No pathological findings were made out by the physician who was called, the vomiting ceased on the following day, and the patient could again see and speak. He complained of a strange and uncomfortable feeling in his chest, and 48 hours after the onset, he suddenly died.

The necropsy showed a dissecting aneurysm of the aorta extending from above the valves of the left common carotid, and a rupture into the pericardial sac. In this man the aortic wall appeared healthy, but there was a slight degree of stenosis of the aortic valve and the left ventricle was hypertrophied.

Case 4 (16).—A woman, aged 63 years, suffering from dementia, had been physically robust, accustomed to brisk walks in all sorts of weather, until overtaken by apoplexy, following which, while at rest in bed, she had repeated attacks of pain in the chest diagnosed as angina pectoris.

Following the necropsy, the additional history was obtained that 18 years before the date of death, the patient had been thrown from a sleigh, striking on her head and becoming unconscious, and for two months had been confined to the bed. Three months after the accident, there was an attack of loss of consciousness. Shortly after the pyschosis developed, and occasionally she showed mild circulatory weakness.

There was found generalized arteriosclerosis, with an area of hemorrhagic degeneration in the right corpus striatum, and a dissecting aneurysm extending from the arch to the coeliac axis, where through a second rupture the outer channel joined the aortic lumen. The aneurysmal wall was smooth and lined by intima. In the ascending arch there was a small adventitial tear, 1.5 cm. in its largest diameter, containing coagulated blood.

Case 5 (3).—A man, aged 52 years, was in good health until an attack, after he had eaten breakfast and was starting for work, of syncope, cold sweat, pallor, cyanosis, subnormal temperature, and the disappearance of both radial pulses.

After digitalis, the right pulse returned, while the left arm felt "very heavy." Hemiplegia was absent.

Four hours after the attack, there was severe pain in the heart and in the upper back. The left pulse could now be felt, but there was marked inequality. The right brachial blood pressure was 200/100 mm., the left 100/60. The heart was enlarged to the left, regular, rate 70 beats per minute. Strong spontaneous pain continued in

the back, radiating forward encircling the chest.

The white blood cell count was 14,500, the Wassermann test negative.

The clinical diagnosis was made of dissecting aneurysm of the aorta and left subclavian artery.

Six days later, after an interval of almost complete well being, the patient died suddenly.

The dissection extended from the first portion of the arch to the bifurcation of the aorta, and all the intercostal arteries had been amputated. Hemopericardium was present.

Analysis of these cases, and of numerous other equally interesting and characteristic records, leads to the emphasis of four primary clinical features of dissecting aneurysm: (1) the mode of onset; (2) the character, distribution, and duration of pain; (3) the occurrence of abnormal circulatory phenomena; (4) the effects of disturbances of circulation in other organs or systems of the body.

The presence of pathological conditions which predispose to an intimal rupture, such as hypertension, arteriosclerosis, dilatation of the aorta, is important in a given case, and the absence of clinical or serological evidence of syphilis has a certain value in favor of dissecting, as against saccular, aneurysm.

Clinical Features of Dissecting Aneurysm

(1) The onset is characteristically sudden and abrupt. It follows at once or within a few hours many forms of physical strain. A young man dances all night, goes to bed, and the pain of rupture of the intima ensues. A woman carries a sack of potatoes, a workman supports a heavy stone, an oarsman indulges in a sprint: there follows pain, or a sense of something giving way. While the digestive and circulatory systems are coping with the burden of a meal, many attacks begin. During vomiting, coughing, defecation, the primary tear may take place. Trauma—a blow, a fall, even the action of extending the arms in yawning,—may set off the process. Psychic factors are not uncommon.

The first symptoms may be relatively mild—a sense of discomfort, or of oppression in the chest. Syncope is common, in some instances clearly due to cerebral anemia from obstructed or diverted blood supply. Nausea, vomiting and weakness often occur at the onset.

(2) The pain of dissecting aneurysm is its outstanding symptom. It is described as violent, sharp, knife-life, tearing, "as if something within the chest had broken." Its segmental distribution is likely to be higher than the pain of coronary artery disease—its radiation may be down the outer, and not the inner, side of the arm. It is constant and continuous, like the pain of coronary artery occlusion, and equally resistant to all drugs save morphine.

With the progress of the dissection, the simultaneous appearance of pain in the back of the chest (tearing of the intercostal arteries in some cases), in the abdomen, or in the lumbar or sacral regions (obstruction to the dissection at diaphragm, abdominal arterial trunks or bifurcation), is of particular diagnostic significance. The symptoms may suggest perforated gastric ulcer or a gall bladder attack, and the evidence of circulatory

versus gastrointestinal disease must be weighed. It is worth noting that dissecting aneurysm may be accompanied by a marked leukocytosis.

(3) Among the circulatory changes distinctive of dissecting aneurysm the presence of a harsh, rumbling, or hissing systolic murmur over the heart and great vessels has been recorded. Inequality of the pulses, or their absence in various domains—the arm, one side of the neck, the lower extremities—are important evidence of compression or occlusion. Bilateral blood pressure determinations are helpful under these conditions. The appearance of adventitious enlargements within the thorax, in the neck, or along the abdominal aorta, accessible to palpation or percussion, or revealed by X-ray, have been clues to diagnosis.

(4) Interference with the cerebral blood supply is frequently associated with dissecting aneurysm, and the complete obstructions to carotid circulation which may thus arise may be responsible for encephalomalacia, hemiplegia, and death. Coronary circulation is less often interrupted. Compression of the renal arteries has been seen to precede anuria, and characteristic renal pain. In cases of abdominal distention, with ileus, pressure of the dissecting-aneurysm on the splanchnic nerves has been considered.

Extravasations of blood follow in the path of the damage done by dissecting aneurysm to the aortic wall or the circulation in its branches, and have produced hemoptysis, hematemesis, and hemorrhage into the intestine. Hemoglobinuria has been found. Gangrene of the foot has followed obstruction to the femoral artery, and paraplegia resulting from meningeal bleeding has been noted as one of the more remote phenomena caused by dissecting aneurysm.

In Goodman's (17) patient, a man of 40 years, who recovered, dyspnea, severe pain in the upper chest which followed unusual physical strain, a left hemothorax, and aneurysmal dilatation of the aorta, with no history or evidence of syphilis, and a negative Wassermann blood test, made up a picture which meets these clinical criteria convincingly.

Summary and Conclusions

Dissecting aneurysm of the aorta is a remarkable and well known pathological condition, of which over 400 cases are recorded. In only a handful of patients has the disease been recognized during life. This disproportion challenges clinical attention.

Analysis of the clinical features and course shown by patients with dissecting aneurysm yields a syndrome which in certain groups of cases can be considered characteristic. These features are: a sudden onset, usually following strain; pain, which is severe, continuous, and often with significant distribution; anomalies of the circulation; remote effects from disturbances of blood supply in other organs or systems of the body.

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Ulcerative Endocarditis of the Pulmonic Cusps*

Case Report

By Edward Weiss, M.D., *Philadelphia, Pa.*

L. S., a colored woman of 34, was admitted to the Jefferson Hospital in the service of Dr. Thomas McCrae, January 24, 1928.

She complained of pain in the right chest, chills, cough and expectoration. The family history was negative. The past history was unimportant. The patient had one son nine years old and had three miscarriages prior to the birth of her son.

The history of the present illness was not quite clear. Apparently it began late at night on January 18, with pain in the right chest posteriorly, but there was some history of two attacks of chills a week or two before this time. The pain in the chest increased the following day. Cough began about January 21. There had been repeated chills since the beginning of the illness.

Physical examination showed a very sick, obese, colored woman, with marked dyspnea. The temperature was 103, pulse 112, and respirations 30. The apex beat was in the fifth interspace almost to the anterior axillary line and left ventricle dulness extended to that point. There was a systolic murmur at the apex which, however, was loudest in the third interspace to the left of the sternum and at that point had a rough quality like a pericardial friction rub. It also was heard in the pulmonic area but not to the right of the sternum. The upper portion of the right lower lobe posteriorly gave evidence of consolidation. There was dulness on percussion and distant tubular breath sounds with small moist râles. Otherwise, the physical examination showed nothing of importance.

The blood pressure was 190/74; the blood count, hemoglobin 50 per cent; red blood cells 3,100,000; and white blood cells 30,000. The urine showed a cloud of albumin, a large number of white blood cells, many red blood cells and many granular casts. The sputum yielded group IV pneumococcus. The blood Wassermann was negative.

The clinical picture was not definite. It was thought that there was an atypical pneumonia of the right lower lobe complicating a heart lesion. On January 27, three days after admission, the temperature suddenly dropped almost to normal but the pulse remained about 120 and the respirations 28. Physical signs were unchanged over the lungs but the character of the murmur heard over the body of the heart seemed somewhat different in that it was distinctly to and fro with the diastolic element very pronounced. Together with the great disparity in the systolic and diastolic pressures which now were 185 and 60, and a very suggestive collapsing pulse, it seemed that the heart lesion was probably aortic regurgitation.

The urine continued to show albumin, blood and casts, and chemical analysis of the blood, which showed slight nitrogen retention on January 27, showed very marked retention on January 30; the urea-nitrogen was 120 mg. and the creatinin 9.6 mg. The carbondioxide combining power of the blood was 30.5. The blood culture was negative at the end of 48 hours.

*From the Department of Medicine, Jefferson Medical College Hospital, Philadelphia.

Following the drop in temperature on January 27, there was apparently slight improvement but soon the patient became drowsy, then stuporous and finally comatose on January 30. The conception of the clinical picture at this time was: probable aortic regurgitation, pneumonia (or infarct) of the right base and a complicating acute renal lesion (possibly engrafted upon an older process) leading to uremia.

The patient died on January 31. Autopsy (Dr. B. L. Crawford) revealed a pneumonic area in the middle portion of the right lower lobe posteriorly, chronic nephritis and ulcerative endocarditis of the pulmonic valve. Portions of two cusps were ulcerated but the vegetative lesion had neither the appearance of being very acute nor apparently had it been engrafted upon chronically diseased valve cusps. Smears from the vegetations did not show organisms. Microscopic sections of the vegetations revealed necrotic tissue with groups of polynuclear leukocytes and occasional fibroblasts but no mass of organisms. Only a few gram-positive diplococci were seen in properly stained sections. Postmortem blood culture was negative. The left ventricle was somewhat hypertrophied but otherwise there were no additional lesions of the heart. Microscopic examination of the lung showed a fibrinous pneumonia, and of the kidney an acute exacerbation of chronic glomerular nephritis.

It is difficult to say with certainty what the sequence of events in this case was. Did the pulmonary valve endocarditis complicate the pneumonia or was the period of illness with vague symptomatology preceding the onset of pneumonia caused by endocarditis. In the latter event the pneumonia might be explained on the basis of an embolus from the pulmonic orifice. Unfortunately microscopy did not aid materially in determining the age of the vegetative lesions. It is more than likely, however, that the endocarditis was a complication of the pneumonia. The chronic renal lesion must have been responsible for hypertension and left ventricular hypertrophy, and renal insufficiency seemed responsible for death. The unusual localization of the vegetative endocarditis, the difficulty in determining whether it was primary or secondary, and the fact that it was considered clinically to be aortic regurgitation are the special features of interest in this case.

Albuminuria and Nephritis Following Injection of Toxin Antitoxin*

With a Report of Two Cases

By C. D. Mercer, M.D., F.A.C.P., *West Union, Iowa*

IMMUNIZATION of school children against diphtheria with Toxin-Antitoxin has been undertaken on a wholesale scale in Iowa. The physicians of our little city were asked to give these injections, working in relays at the school building, using a stock serum manufactured by a well known firm, and supplied by the State Board of Health. Having fresh in my mind an article by Gersterley (1) reporting a sudden death from nephritis in a child who had been immunized, I asked that the children be sent to their own physician where a suitable history could be taken and physical examination made.

One hundred twenty five children between the ages of six and twenty appeared for immunization. Thirteen or 10% had albuminuria without other symptoms of nephritis. Hess (2) states that 10% of boys and 20% of girls show this condition during stages of their development. More than 50% of the children in this group had enlarged tonsils and adenoids. The children were given 1 cc. of the stock serum at seven day intervals for three doses. After the third injection 27 or 20% had albuminuria.

Case Reports:

L.R., aged 7, with enlarged tonsils and adenoids, anemic and poorly nourished, was examined Dec. 5, 1927 and found to be free from albumin. He received three injections of the T-A mixture at seven day intervals, receiving the last injection Dec. 19, 1927. Two weeks later he was admitted to the hospital with the following symptoms: Generalized edema of his whole body. Hemoglobin 70%, RBC 3,200,000, WBC 5000. Blood pressure 115/80. Urine—Sp. Gr. 1020, albumin 4 plus, sugar negative, many hyaline and granular casts. PSP 40. Non-protein-nitrogen 46.4 mgs. per 100 cc. blood. Wassermann negative. Patient was put in bed, kept warm and given an O'Hare (3) nephritic diet. Intake of fluids restricted to output. On Feb. 6, 1928, 2500 cc. fluid was withdrawn from abdomen. Edema, ascites and hydrothorax with albumin and casts in urine continued until Feb. 12 when symptoms began to clear up. On Feb. 17 there was no edema, albumin or casts present. Albumin without edema re-appeared Feb. 26 and continued until March 13. On March 30 patient left the hospital free from edema and urinary symptoms. PSP 75. Patient has remained free from symptoms up to the present time July 1, 1928.

R.C. was admitted to the hospital Jan. 18, 1927 with a diagnosis of chronic nephritis. Age 20. Had scarlet fever at age 8 and has had trouble with kidneys most of life. Had a mastoid infection at

*From the West Union Community Hospital.

age of 16 which was not operated but allowed to go on to necrosis of bone. This discharged for several years but finally healed. Physical findings: Hemoglobin 60%, RBC 3,850,000, WBC 6000. Urine: Sp.Gr. 1015, albumin 2 plus, sugar negative, showers of granular casts. Creatinin, 1 mgs. per 100 cc. blood, Urea nitrogen, 15 mgs. per 100 cc. blood. PSP 35. Wassermann negative. Blood Pressure 260/120. Patient was given routine treatment for thirty six days and left the hospital with a negative urine. Returned in seven days with a very severe Vincent's Angina. Recovered after two weeks and again left the hospital with a negative urine. Patient remained free from symptoms during the summer and gained sixteen pounds in weight. In September she was given three injections of a stock T-A mixture at seven day intervals. Within a few days after the last injection albumin re-appeared in the urine. She had another attack of Vincent's Angina in December and was admitted to the hospital again April 5, 1928, very ill. Sp.Gr. of urine 1005, albumin four plus, granular and hyaline casts and some pus. PSP 30. Creatinin, 5 mgs. per 100 cc. blood. Urea nitrogen, 27 mgs. per 100 cc. blood. Blood pressure 260/160. Hemoglobin 60%, RBC 3,200,000, WBC 20,000. Patient died April 18, 1928. No autopsy could be obtained.

Rhoades (4) after a study of the protective value of stock preparations on nurses in Cook County Hospital, emphasizes the necessity that the preparations should be carefully controlled.

Experience in this group of children would seem to show that either more refinements are needed in the manufacture of the preparations or the profession should also study the toxic effects more closely before it is given in a wholesale way, or both.

Summary

1. A great many apparently healthy children have albuminuria.

2. Administration of T-A doubled that percentage in 125 school children.

3. Urine examinations should be made in all cases before immunization.

4. Until the manufacturers furnish a better preparation it should be given with caution.

5. Potential nephritics, patients with remission nephritis and children with throat trouble should not be given stock serum without careful study.

6. Toxin-Antitoxin is not "A harmless preparation" and should not be given school children in a haphazard way.

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Report of a Case of Complete Heart-block with Autopsy Findings

Syphilitic Myocarditis and Aortitis

By Walter J. Wilson, *Detroit, Michigan*

F. A.B., physician, aged 44; married; parent of two apparently healthy children, ten and five years of age respectively.

Parental History: Father living and well at 70 years; mother died at 68 years of carcinoma of the rectum and an associated auricular fibrillation and cerebral thrombosis. There is a history of two brothers living and well.

Personal History: Army service: At one time had a sore tongue; had a peculiar sensation in the heart after an eighteen-mile walk and had a systolic blood-pressure of 180 while in the service. Military discharge papers call attention to a peculiar heart-sound.

Past History: There has been no previous illness, except an attack of gonorrhoea in earlier adult life; also an attack of acute rheumatic fever about four years ago. In 1921 an X-ray picture was thought to show a knob on the aorta. In 1924 a heart murmur developed. In 1925 he entered a sanitarium on account of stiffness of the joints. Each time that he took a bath, he had an attack of syncope. When seen by me December 1, 1925, examination showed cardiac enlargement, enlargement of the aortic area, muffled first sound and the second aortic sound was replaced by a diastolic murmur. The blood Wassermann at this time was reported XXXX.

Recent History: When seen again August 3, 1927, the blood-pressure was 230/80, pulse rate 48, heart rate 46 with one premature beat per minute. X-ray examination showed marked aortic enlargement and a duck-shaped heart. The electrocardiographic record showed complete heart-block, two beats of the auricle to one of the ventricle with widening of the RS interval and signs of left bundle-branch block, together with a number of premature systoles. The patient was at this time sent to St. Mary's Hospital for observation. From then on, the pulse-rate was at various times 30 to 52. He had had during a few weeks previously different heart attacks with loss of control of the lower extremities. At times he lost control of his automobile, driving it into the ditch; however, he did not lose consciousness. About Sept. 1, 1927, two blood Wassermanns at different laboratories, were XXXX. The patient died on Oct. 9, 1927. Previous to death, he had Cheyne-Stokes respiration.

Physical Examination Sept. 10, as on Hospital chart: White adult male, lying quietly in bed with a back-rest and in no apparent pain, although there is a look of apprehension on his face. *Head, eyes, ears and nose*—negative. Mucous membrane: Fair color. Teeth: Good condition. Neck: No palpable glands, no enlargement of the thyroid. Chest: Well developed and well-nourished, moves well and equally on respiration. Reasonance throughout, breath sounds vesicular throughout, no râles heard.

Heart: Apex beat not seen; on palpation the apex beat is lapping in character. The heart sounds are of poor quality, a double murmur being heard over the whole precordium but more marked in the aortic area. There is a systolic murmur in the mitral area. The blood pressure is 180/80. The radial vessels are not thickened. The rate is 51. The pulse rises quickly and is not maintained but falls quickly. The

pulse on the right side is stronger than that on the left, which seems to be slightly retarded. Owing to soreness of the left arm, the blood pressure was taken only in the right arm.

Abdomen: Well-developed, well-nourished, moves freely on respiration; liver, spleen and kidneys are not palpable. No masses were felt, no areas of tenderness.

G.U. Negative.

Extremities: Negative.

Reflexes: Present, equal, active.

Laboratory Findings: Sept. 11, 1927.

Urinalysis: Color, amber, clear; reaction acid; specific gravity 1.022; no albumin, no sugar; an occasional W.B.C.

Blood Wassermann: XXXX positive.

Blood-count: WBC—800; polys 71%; small lymphocytes 27%; abnormal 1%.

September 22, 1927.

Blood-count: Hemoglobin 80%; index 1.02; R B C 3,900,000; W B C 9,400; polys 76%; small lymphocytes 33%; abnormal 1%.

Therapeutics: Barium chloride was used in doses of 1/15 gr. three times a day, without any apparent effect on the heart-rate. Sodium iodide was introduced intravenously throughout the time of observation, fifteen grains usually being given. On one occasion, when introducing 31 grains rather slowly, short periods of cardiac asystole were noted and thereafter, the dose used was never above fifteen grains. Atropine sulphate in dosage of 1/100 grains was given but simply seemed to distress the patient in general, without any change in the heart-rate. Mercury salicylate, dosage one grain, was given once a week.

An autopsy was performed by Dr. Jas. E. Davis on October 10, 1927. The report follows:

Note: Positive findings only recorded.

Subject: Well-nourished, fairly stout body, florid complexion.

Thoracic Cavity: The heart is enlarged; the left ventricular thickness 3 cm. Weight of the heart with aorta, 940 grams. The papillary muscles are enlarged and sclerosed. The chordae tendiniae are enlarged and fused. The mitral valve is thickened and sclerosed; physiologic approximation is doubtful as the valve assumes a circular and fixed position when natural approximation is afforded. The right ventricular cavity is small, the wall being 1 cm. thick. The tricuspid valves are normal. The pulmonary parts are negative. The aortic valve opening is large; the leaflets have a low attachment and the middle leaf is greatly increased in length to approximately 4 cm.; the leaflet is thickened and extensively calcified. The coronary vessels are enlarged, their walls stiffened. The atrial walls show some fibrosis and thickening and the area of Keith and Flack is definitely sacculated—circumference 13.5 cm. The distal aorta has a circumference of 5.5 cm. There is a diffuse atheromatous degeneration, which extends up the larger neck vessels with a marked lesser degree of involvement.

Abdominal Cavity: The spleen is enlarged and fibrosed—weight 310 grams. The kidneys are of enormous size, show slight cloudy swelling, early atrophy, arteriosclerosis and sclerosis of the apices of the pyramids; there is an increase of pelvic fat. One kidney weighs 180 grams, the other 190 grams.

Microscopic Examination:

Microscopic sections were taken as follows:

1 section from lower part of thoracic aorta.
1 section from area of the pacemaking node of Keith and Flack.
1 section from left ventricle.
1 section from papillary muscle, left ventricle.
1 section from proximal aorta.
1 section from carotid artery.
1 section from coronary artery in the right ventricle.
1 section from kidney, including cortical cyst.
1 section from each kidney.
1 section from splenic artery.

Microscopic Report: Arterial Wall: Exhibits a very marked sclerosis, particularly of the adventitial vessels together with some round-cell infiltration in the adven-

titia. There is marked degeneration of the elastica; the intimal margin is irregular and frayed. Another section of the artery shows small round cell infiltration on the intimal surface and fatty degeneration. Another section (artery) exhibits marked calcification and there is early myxomatous degeneration of the connective tissue. Still another section of artery shows masses of lymphocytes infiltrated about adventitial vessels; also degenerating areas in the intima and media with repair tissue and small round cell infiltration in these areas; the intima is irregularly piled up and markedly degenerated.

Heart Muscle: Shows patchy sclerosis and small round cell infiltration on the epicardial surface and there is an epicardial vessel with a greatly thickened intima. There is an infiltration of small round cells in the interstitial tissue. Another section of heart shows degenerative changes, irregular hypertrophy, large areas of interstitial tissue increase. Still another section shows an area on the endocardial surface diffusely infiltrated with small round cells, partly degenerated and extending up to the valve portion; there are numerous patches in this section in the middle of the heart muscle, showing small round cell infiltration and productive connective change.

Kidney: The vessels exhibit sclerosis and some vacuole production. The kidney capillaries are congested and the kidney capsule is thickened and adherent. There are patchy areas of old parenchymatous degeneration. In another section the arteriosclerosis is extremely marked, there is perivascular small round cell infiltration and there are some cysts in the corticular portion as well as in the pyramidal portion.

Spleen: Shows marked congestion and atrophy of stroma.

Specific stain (*Levaditi*) for Spirocheta pallida: Positive. Spirochetes were found in the inter-ventricular muscle septum just below the base of the aortic valve, cutting in at right angles in the long diameter of the heart.

Diagnosis:

(1) Syphilitic myocarditis and arteritis.
(2) Syphilitic valvular endocarditis.
(3) Sclerosis of pathway tissues of His bundle conduction stem.

Comment: The correlation of data in this case gives an agreement in all details. The alignment of these details being as follows:

(1) Repeatedly positive blood Wassermanns.
(2) Typical clinical cardio-vascular pathology, with extension from the aortic valve by the interventricular septum so as to involve particularly the stem of the His bundle.
(3) Descensus of segment attachment of the aortic valve.
(4) Classical structural changes in the large vessels, vasa vasorum and myocardium.
(5) Presence of spirocheta pallida in the tissue.

Scarlet Fever*

By A. R. Dochez, M.D., *New York City*

I WANT to talk to you about certain questions related to the pathogenesis of scarlet fever. As you know, this disease has always been of extraordinary interest. All you have to do to see how perplexing it has been is to consider the history of its epidemiology. At times it appears as a devastating, plague-like infection, decimating whole communities. There are histories of epidemics on record where the case fatality rate has been over 30 per cent. A number of years later it subsides into a fairly mild infection. In this country today the case fatality rate in many localities is 1 per cent. That condition of affairs exists over a large part of the world, but it is not true throughout the entire region of its incidence. In Russia, for instance, and in some of the southeastern countries of Europe the case fatality rate is still high in certain localities. In China, especially among the Chinese, it can assume a plague-like character. It wipes out whole families and it has always been very perplexing to understand how an organism could vary so much in its virulence in relatively short periods of time. There are those who believed that racial immunity has risen to such a point that epidemics with high case fatality rates are unlikely ever to occur again. However that may be, we still have to consider the threat it offers and devote our time and attention to the study of this disease.

Considerable progress has been made over a period of many years. It began long ago in Austria, and has been carried forward in Russia and other places. I will not leave scarlet fever before calling your attention to the hypotheses of recent years, and certain modifications of these hypotheses which are in course of development today.

As you know the clinical manifestations of scarlet fever present many interesting problems. In the first place, there is a local infection of the throat, more or less severe. It may be simple swelling and edema, with slight exudate, or it may develop to an extensive necrosis, with sloughing. This inflamed condition of the throat goes on for a short time and then there appears a generalized toxic eruption of severe character. This lasts for a varying time, perhaps two days, perhaps six days, and then disappears. With the disappearance of the rash the average mild case without complications shows im-

*Informal address as part of a Symposium on Infectious Diseases at the Twelfth Annual Clinical Meeting of The American College of Physicians, New Orleans, La., March 7, 1928.

mediate improvement in the general condition, the fever subsides and the patient feels well. Accompanying this, especially toward the end of this phase, or even after this phase has subsided, there appear certain septic complications. These are, as a rule, simple extensions of the local condition in the throat. The condition may extend into the respiratory tract from the tonsils, into the regional lymph glands, and from the lymph glands into the tissues of the neck, where it may produce a septic thrombosis of the veins, and from there an infection of the blood takes place and a true septicemia develops. It may establish metastatic foci in other regions, the usual place being in the joints. The septic foci run a varied course. They sometimes disappear quickly and sometime continue for weeks, leading to much difficulty.

Later on in certain cases there may appear quite a different group of phenomena, the nature of which we cannot say is understood today. The most significant of these are the changes which take place in the kidney and those which take place in the heart. In the kidney one gets an acute glomerular nephritis, which may reach a considerable degree of severity and subside, or it may continue for a long time. The subsequent course of these nephritides is not entirely clear, but there are many in which undoubtedly complete recovery takes place. The significance of this process to the future of the kidney is not clear. Much work is being done today in an attempt to throw light on this and determine what changes are produced in the kidney, and in what way they can lead to a continuous and progressive disease.

Regarding the changes in the heart there has been much discussion. You have all heard of scarlatinal rheumatism. This appears during the second or third week of scarlet fever, complicated by a mild arthritis and cardiac changes that occur in acute rheumatic fever. There has been some doubt as to the etiology of this type of rheumatism. The older observers were inclined to believe that there existed in the throat a specific virus, that this was activated by the virus of scarlet fever, and that following the scarlet fever the patient had typical rheumatic fever. Another view, receiving more support today, is that this rheumatism and cardiac disease are part of scarlet fever. That is why I say that this disease presents such extraordinarily interesting questions from the standpoint of general infection and pathology of the infectious process. It is a difficult problem to discuss, and I do not wish to give too much time to it. I do want to say enough to show how points of view are changing in regard to the nature of the infectious process in scarlet fever.

You may remember that scarlet fever has been likened to diphtheria, more particularly recently, but this idea is not new. It was emphasized by Bergé as early as 1895, and also by a Russian investigator who studied scarlet fever in Russia in 1903 and 1908. More recently a very striking analogy between scarlet fever and diphtheria was drawn by Mair in England. The most definite thing he brought out was an explanation of the

Schultz-Carlton test. If the test were positive it was found that if the the serum was injected into a patient with scarlet fever the area at the site of this injection was blanched. The previous explanation given for this was that something was lacking in the serum. Mair studied an individual before, during and after scarlet fever. He found that before scarlet fever the blanching substance was absent, and was also absent during the the acute attack, but that during convalescence the serum had the power of blanching the skin. Mair deduced from this that the blanching substance is a specific immune body which develops during the attack, neutralized the circulating toxin and causes the rash to disappear. He was prophetic at that time and said that if an antiserum was ever discovered it would possess the power of blanching the skin during the disease. The analogy to diphtheria has been in the minds of many for a long time. However, it has been made much closer in recent years by the development of the serum that in the first instance appeared to be an antitoxin like diphtheria antitoxin, and by the Dick reaction, which appeared to bear a similar relationship to scarlet fever that the Schick reaction bears to diphtheria. This has been much emphasized in the last two or three years. At first a so-called antitoxic serum was developed, by the injection of horses with the living organism that functioned in the body and produced an antitoxic serum. If this serum was injected intracutaneously in patients with scarlet fever during the stage of active rash, after twenty-four hours the rash disappeared at the injected site and did not reappear. When injected into patients intramuscularly in larger amounts within thirty six hours, there was an amelioration of all the symptoms. Further studies showed that the toxic stubstance circulates in the blood of patients with scarlet fever. Injections of the serum causes the toxic substance to disappear from the blood and the patient's serum acquires the power to blanch the rash in an active case of scarlet fever.

In addition to these observations Dr. and Mrs. Dick have shown that the streptococcus of scarlet fever produces a substance which gives a specific reaction in the skin. Studies of the nature of this reaction seem to indicate that it is similar to the Schick reaction in diphtheria. If normal individuals are tested to the reacting substance there is a variation in susceptibility. A certain proportion are positive and a certain proportion negative. As life goes on the period of greater susceptibility to scarlet fever is past. As this takes place the incidence of positive reaction diminishes and the disappearance of the reaction is interpreted as indicating immunity to scarlet fever. Furthermore, the first studies indicated that the Dick reaction in general was positive at the beginning of an attack of scarlet fever but during the course of the disease became negative indicating the production of antitoxin by the infected individual. It was also found that individuals giving a positive Dick reaction and presumably, therefore, susceptible to scarlet fever, could be inoculated subcutaneously with increasing amounts of the toxin and after a certain length of time the skin reaction could be

rendered negative and in this manner the individual could be actively immunized against scarlet fever. Studies by Zingher indicated that the Dick reaction in young infants resembled the course of the Schick reaction very closely in that there appeared to be a hereditary transmission of antitoxin from mother to child and that antitoxin thus inherited was present in the child for a limited period of time. These studies seem to indicate a close analogy to similar phenomena observed in diphtheria.

However, as time went on and studies of the relationship of the toxic substance to scarlet fever were multiplied some doubt arose concerning the exactness of the analogy to diphtheria. In the first place, the so-called toxin was heat stable and required boiling for two hours to destroy it completely. It was also found that large amounts of the toxic substance could be injected into guinea pigs, rats and other animals without producing serious effects. Furthermore, it could be extracted from the bodies of the streptococci themselves. Other important discrepancies developed between the Schick and Dick reactions. It was shown that the Dick reaction in infants under six months of age are in general negative if relatively small amounts of toxin are used regardless of the presence or absence of antitoxin in the blood. As time goes on they tend to become positive and there is a progressive increase in sensitivity which reaches its maximum somewhere between the fourth and tenth years. In many instances the reaction becomes negative in scarlet fever sometime before the appearance of demonstrable antitoxin in the blood. Furthermore, in certain individuals the reaction remains positive even after the acute attack of scarlet fever has subsided. Some interesting observations in relation to these phenomena have been made by Brockman. He has been able to cause the disappearance of a positive skin reaction within from twenty-four to forty-eight hours by subcutaneous injection of considerable amounts of toxin. Such an early disappearance of a positive reaction, of course, cannot be dependent upon the production of antitoxin but is more of the nature of a desensitization phenomenon such as is observed in instances of allergy. Brockman furthermore observed that individuals with a negative skin reaction could be made positive by injections of small amounts of toxin and a sensitiveness thus induced. All this work has been corroborated in animals. Laboratory animals give a negative skin reaction upon injection of a toxic substance. They can, however, be sensitized either with filtrate toxin or with the bodies of the organisms themselves. When this has been done the skin reaction becomes positive and such a positive skin reaction can readily be neutralized by scarlatinal antitoxin. There is no doubt that the skin reaction in animals is a hypersensitive phenomenon and that this hypersensitive reaction can be neutralized by an antiserum, the first example of such a phenomenon with which I am familiar. In animals also a positive skin reaction can be caused to disappear rapidly by a single intravenous injection of the filtrate substance. After the lapse of a certain

length of time the skin reaction in animals may again become positive and the whole series of events may be repeated. Somewhat similar observations have been made in human beings in that negative reactions have been observed to become positive and the negative again. These observations would seem to indicate that there are certain fundamental differences between the pathogenesis of scarlet fever and diphtheria. The so-called toxin of scarlet fever is in some ways similar to tuberculin and the positive skin reaction observed on the intracutaneous injection of scarlet fever streptococcus filtrate would seem to be dependent upon hypersensitiveness of the skin of this substance. It differs, however, from tuberculin in that upon injection into animals it gives rise to a neutralizing antibody. We now know that many bacteria give rise on growth in culture to similar filtrate substances. Some of these can readily be neutralized by antisera and others cannot. We now believe that the rash and acute toxic manifestations of scarlet fever are partly dependent upon the existence of a hypersensitive state in the infected individual. Very young children are insensitive to the products of the streptococcus of scarlet fever and therefore cannot have a typical attack which is characterized by the peculiar rash of scarlet fever. After a lapse of a certain length of time they seem to become sensitive to the products of streptococcus and if while in this sensitive state they become infected with a suitable organism may have a typical attack of scarlet fever. As the individual becomes older repeated exposures to streptococci of one kind or another would seem to induce the production of a neutralizing antibody which from then on continues to circulate in the blood. When this state has been reached sufficient antibodies are usually present in the blood to prevent the appearance of typical scarlet fever, even if such an individual should become infected by one of the more highly toxic forms of streptococcus. These observations in scarlet fever have led to the formulation of certain interesting hypotheses in connection with infectious disease. They have centered interest upon the chemical contituents of bacterial cells and have led to the belief that an infected individual may respond in a highly specific way to each of the different chemical constituents of a micro-organism. The nature of the response to one such constituent may be so different from the response to another that the two series of events might even be looked upon as two quite different diseases. We might even think that one series of events would be quite definitely limited in time whereas the other may extend by a series of repetitions throughout the life time of the individual. Whether or not these studies will lead to a better understanding of the relationship of chronic degenerative types of disease to infection remains for the future to decide.

The Relation of Chemical Influences, Including Diet and Endocrine Disturbances, to Epilepsy*†

By H. Rawle Geyelin, M.D., *New York City*

I HAD expected to speak in relation to epilepsy and endocrine disease, but the work along this line has not reached a stage where it is suitable to report it. I will, therefore, limit my remarks to three subjects: First, the effect of fasting and the ketogenic diet upon the course of epilepsy; sceond, the effect of the fasting and ketogenic diet upon the acid base equilibrium, and, third, I will tabulate the results of therapy as I have outlined it, with the old attempt to offer a tentative new classification of this condition.

Work was begun by us on the treatment of epilepsy in the early part of 1919. It was suggested by the results obtained by an osteopathic physician, Dr. Conklin, in Battle Creek, who happened to have fasted a young cousin of mine for relief of the condition. The result in his case was 100 per cent successful in arresting epilepsy over a four year period. Since then repeated fasts have been without avail, and the disease is rapidly becoming more severe.

The first case we undertook for treatment was that of a child who had had epilepsy, both *petit* and *grande mal* attacks, at least ten to fourteen a day for fourteen months. The patient was a boy, aged 9, who was put on complete starvation after two weeks on general diet in a hospital. On the third day of the starvation he went into complete acidotic coma, from which he was pulled through on glucose injections. Since that date, about February 4, 1919, the patient has remained free from minor and major fits. Unfortunately for the others, the same results have not been obtained. We have now, at the end of nine years up to January 1, 1928, no case which we consider cured.

No cases are reported, whether a case on fasting or ketogenic diet alone, or with fasting, or considered an arrested case until at least a year has elapsed. I admit this is an arbitrary way of looking at it, but it helps to explain the great divergence in results that have been obtained by other men who have employed this treatment, Wilder, Talbot, Peterman and Helmholz. The percentage of good

†Proof submitted to author but not returned, Editor.

*Informal address as part of a Symposium on Epilepsy, at the Twelfth Annual Clinical Session of The American College of Physicians, New Orleans, La., March 7, 1928.

results in children is much higher the earlier the results are tabulated in the course of the disease after treatment.

Since 1919 we have personally observed in the hospital and in the office 377 cases of epilepsy. These were only diagnosed as epilepsy after a competent neurologist gave a negative report as to the presence of any other condition, and X-ray examination of the skull showed nothing suggestive of anything other than idiopathic epilepsy. In all but six of these cases the original diagnosis seems to have been established by the subsequent course. The total number treated was 117; those by the ketogenic diet and by fasting, or by fasting alone numbered seventy-nine. The patients were about evenly divided between the two sexes. Of these seventy-nine, fifteen only remain arrested cases today. Six of those fifteen, nearly one-half of the total number of arrested cases, received no treatment other than one period of starvation lasting from three to fifteen days. We have not considered any patient a child who is over fifteen.

Among the remaining cases in this series of 377 there were several adults. Only one adult has had his epilepsy permanently arrested for a period of over two years, and that was interrupted by the fasting. She has now been free from any attacks for seven years. She received a five day fast and then went free for six months, had one major seizure, and since then has had no attacks.

In addition to the fifteen cases reported as arrested in the 115 children, aside from the seventy-nine, in the thirty-eight remaining various forms of treatment, luminal, bromides, anti-constipation procedures, potassium borotartrate, enucleation of the tonsils, and so on, have been carried out. I have recorded one case as treated by meningitis, meaning that subsequent to an attack of cerebrospinal fever the child had no attack for four years. Three of the patients had complete arrest for two years from correction of constipation alone. One case was interesting in this respect, in that the attacks stopped as soon as two regular bowel movements a day were secured instead of a single one. Two patients have remained apparently cured as the direct result of enucleation of tonsils. Six of the fifteen arrested cases have had no ketogenic diet.

Our low percentage of arrested cases, which range from two to nine years, is not in accord with the results reported by Helmholz, Peterman and Talbot, but I think the time elapsed with all these investigators has not been sufficiently long to judge as to whether or not the percentage of arrests will remain as high as at present. For instance, in the report of Dr. Talbot there are twelve cases in children who were selected for this treatment in that they showed no evidence of mental deterioration; our cases were not selected from that point of view, and nine out of the twelve remained completely arrested from three to nine months, which about covers the period of their observation. On the contrary, Helmholz reports 291 children on a ketogenic diet under observation for five years, and reports but 40 and 42 per cent good results. Our own series gives

an arrest in about 20 per cent. I think when the other series have run for longer periods the percentage will be about the same.

This does not sound like a very impressive therapeutic achievement, but when one considers the results obtained by other means than fasting and ketogenic diet, which may be spoken of as our control group, there has been no other case arrested. We have not consciously picked for fasting and the ketogenic diet those children without mental deterioration or other stigma, including family history. We have tried to have the same number of cases of what were looked upon as hopeless receive the ketogenic and the other treatment. The contrast then between the groups is rather striking, but an arrested epilepsy even over periods as long as ten or fifteen years does not give any key to the cure of the disease, and I am dubious as to what the future will bring forth in regard to the disease.

Another thing is the administration of the ketogenic diet. It is a very hard diet to keep up over long periods with the majority of children and the order of intelligence of their parents, as other observers have noted, so failure to achieve results with this diet is undoubtedly, as Helmholz pointed out, due to inability to stick to the diet.

In searching for some explanation as to why the fasting seemed to have some effect and the ketogenic diet had also, two theories have been proposed by the men who have employed this treatment. Some have felt that it was due to acidosis, and that if they could produce an acidosis they could control the number and severity of the seizures, while producing an alkalosis would tend to produce seizures. Dr. Kalb and myself have been able to bring about seizures during starvation when this had apparently stopped the seizures. We have been able to bring on a complete reversion to the epileptic state by giving large doses of sodium bicarbonate. However, it is quite plain that the treatment is not responsible for the condition observed. This is brought out by the fact that producing a ketonuria does not affect the course of the epilepsy. In one instance it apparently did for ten weeks, but in others no results were achieved. Dr. Wilder believes that the diacetic acid is capable of producing an ether-like radical and that this acts as an anesthetic on the nervous system. He finds the results when there is an acidosis produced by keto-acids but not when produced by other acids.

In the slide shown the blood hydrogen-ion concentration on two normal individuals is given. You will notice that we have arbitrarily picked 7.34°. and at least 90 per cent of our observations of normal individuals fall within this area. You will see that there is a distinct acidosis at this period (indicated), and after the starvation was over the chart swung as you see it here. There was a greater tendency in the epileptics to have a more varied swing in the hydrogen-ion concentration of the blood.

(Slide) This chart represents the fasting period, and this (indicating) the resumption of attacks on normal diet. You will notice the big swing in the hydrogen-ion concentration, reaching a high degree of acid here

(indicating) and then followed by a big shoot with an outbreak of nine convulsions over a period of four days. Unfortunately, we did not have the hydrogen-ion determinations during the fasting, but we have it here, when it went down 32 volumes in percentage.

(Showing slide) This shows the determination of seventeen normal individuals. The vast majority of these fell within the normal age range, a few on the extreme acid side and a few toward the alkaline side of normal.

In closing, I would like to offer as a suggestion, that we attempt to form a standard, if only from the standpoint of therapeutics, to suggest a new classification of the disease commonly spoken of as epilepsy. If one can judge from the general downward trend in any form of treatment, particularly the failure of certain groups of children to respond to starvation and the ketogenic diet, one is impressed with the fact that this group falls almost exclusively in the mentally deteriorated, in those who owe this to long continued use of bromide and luminal, and those who come under one year of age. These results coincide with those in the other clinics.

It is interesting that in all this series over 92 per cent achieved their epileptic manifestations before the twentieth year. That is in correspondence with Dr. Geyer's statistics obtained in analyzing several hundred cases.

I bring this out only because it shows that we are fairly safe in classifying them during the childhood age, for that group that occupies a percentage of our state hospitals. Perhaps that has something to do with explaining the poor results Dr. Allen had when he fasted sixty epileptics in the New Jersey State Home for Epileptics. The majority of these patients are mentally deteriorated. If we adopt some other term for that group, spasmophilia or what you will, it may be possible to divide that group into three, four or five sub-groups. One would fall into those due to the allergic reaction, another perhaps to instability of the circulatory system, a third small group to endocrine disturbance, and so on. There are other possibilities which time will not allow me to take up, but only by attempting to class our cases in this way will we be able to achieve half way satisfactory therapeutic results, and I think in this way we can simplify investigation as to the etiology of the disease.

Last of all, if the medical profession as a whole, can remove the term epilepsy from the majority of cases of what are today called epilepsy, it will bring great comfort to many individuals. The results of fasting and the ketogenic diet are apparently the best that are obtained by any therapeutic procedure that we have to offer to epileptics in childhood today.

Ureteral Stricture as a Cause of Attempted Suicide*

By Mitchell Bernstein, M.D., *Philadelphia, Pa.*

In view of Hunner's teaching of the possibility of ureteral stricture simulating a variety of acute and chronic abdominal conditions, the following case report of attempted suicide due to the pain of an ureteral stricture, I believe, is of more than academic interest.

Case Report:—

C. R., aged 44, female, married, was admitted to the Jewish Hospital on May 2, 1928, in an unconscious condition as a consequence of illuminating gas poisoning, the gas being taken with suicidal intent. After resuscitation, the patient stated that she attempted suicide since she has suffered unbearable abdominal pain, from which she was unable to obtain any relief, and preferred death to the continued agonizing pain. Her father died of diabetes at 67, and her mother died of carcinoma of the liver at 58. One brother, aged 48, was living and well. There was no history of any mental disease in the family.

Personal History:—

The patient had pneumonia, measles, and whooping-cough during childhood. Menstruation began at 13. She married at 25, and had three children, of which two were twins. One of the twins died at five and one-half months, and the other at 12 years of age.

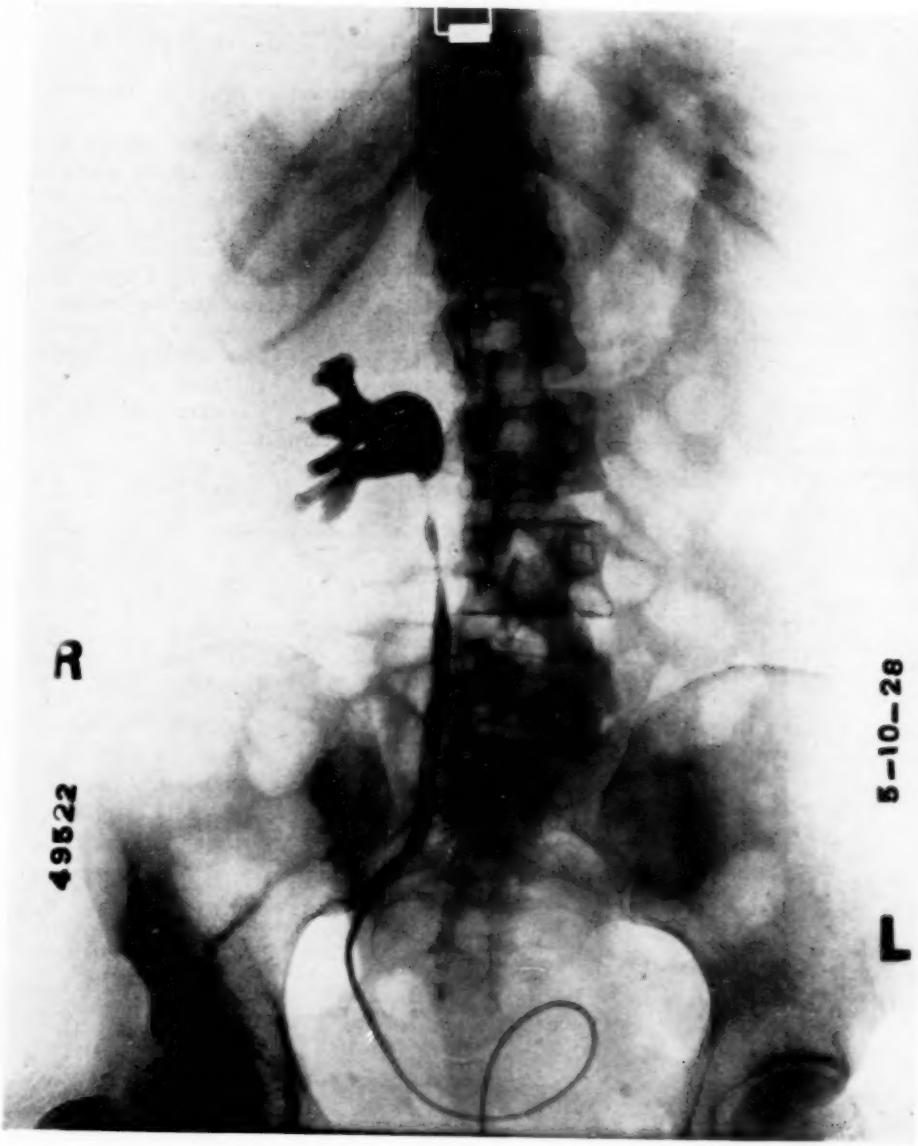
The patient's present illness dates from 1923, when she first developed severe pain in the upper right abdomen. The pain was intermittent in character. It radiated to the back and right shoulder. Nausea and belching always accompanied the attacks of pain, but vomiting occurred only occasionally. A sense of abdominal constriction, beginning at the right upper abdomen, often occurred with the onset of pain. These attacks of pain varied from several minutes to several hours in duration. She was never jaundiced.

In an effort to obtain relief from symptoms, a hysterectomy, together with an appendectomy and pelvic repair was performed sometime in 1923. Operative procedure did not relieve the symptoms. The constant pain following the operation prompted her to consult a number of physicians as well as a number of clinics at various hospitals. She was told she had gall bladder disease, for which she was treated. The various treatments were of no avail, each succeeding attack becoming so excruciatingly painful, the patient became desperate, and attempted suicide on May 2, 1928.

Physical Examination:—

The patient was a fairly well-nourished white female. She had a slightly yellowish pigmentation on forehead and side of the face. The skin was dry and somewhat thickened. The eyes, nose and throat were normal. The neck was normal. Examination of the lungs and the heart proved negative. The abdomen was relaxed and a scar of the previous operation was present. The liver and spleen were not enlarged. There was no tenderness over the gall bladder region. Bi-manual palpation of the right kidney caused a great deal of pain, although the lower pole of the right kidney was barely palpable. The left kidney was not palpable. The reflexes

*From the Medical Service of Dr. Bernard Kohn, Jewish Hospital, Philadelphia, Pa.



X-Ray Plate Showing Ureteral Stricture

were diminished. The blood pressure was 120 systolic, and 80 diastolic.

Laboratory investigations, including examination of the urine, blood, blood chemistry, Wassermann reaction, gastric analysis, biliary drainage, and X-ray of the gall bladder all proved negative.

Comment:—

The history and physical examination suggested the possibility of right ureteral stricture. The ureteroscopic examination, and pyelographic studies confirmed the clinical diagnosis.

The stricture was found at the extreme upper end of the right ureter. (Plate No. 1 shows clearly the site of the ureteral stricture.)

The X-ray report states as follows:

"The opaque catheter extends as far as the inferior aspect of the fourth lumbar vertebra on the right side. There was some dilatation of the ureter in the lower lumbar sacral region, and narrowing immediately before it reached the pelvis of the kidney. The pelvis of the kidney seemed larger than normal. The calices are well-defined, and show nothing abnormal. There was no shadow of calculus seen in the urinary tract."

On May 22, 1928, bougies numbers 4, 5, and 6 were passed the entire length of the right ureter, although resistance was felt to the number six. The patient was relieved following the ureteral dilatation, and was discharged from the hospital May 23, 1928, with instructions to report at stated intervals for continued treatment.

The ureteroscopic examinations were made by Dr. John B. Lownes.

The X-ray studies were made by Dr. Sidney L. Feldstein.

Our Changing Profession*

By Thomas B. Cooley, *Detroit, Michigan*

THESE somewhat random thoughts are the result of cogitation over a questionaire from the Council on Medical Education, which I daresay some of you also received, and to answer which satisfactorily would involve consideration of the history and development of medicine, the past and present status of the medical profession, in itself and in relation to the community, and possible changes due on the one hand to the advance of science, and on the other to developments in the general social structure.

It is the veriest commonplace to say that there has been, within the past quarter century, a very great change in the relations of the members of the so-called learned professions to the other classes of the community, and in the nature of the regard in which they are held. My father, and most of yours, were dignified old gentlemen in plug hats at forty-five; holding themselves, if not exactly aloof, at least a little apart from the merchant, the manufacturer, and the banker, and looked up to by all classes for a real or supposed intellectual and cultural superiority, and in the case of the physician, because of a certain glamor of mystery attendant on a calling quite beyond the layman's ken. This honorable position in the community went far, in the case of the minister and the physician, to make up for the disparity in the financial returns between these callings and the more lowly business pursuits.

Certain modern developments have wrought great changes in all social relations, especially in the United States. The progress of mechanical invention, railway, telegraph, telephone and radio, the automobile and the accompanying road building, have made communication universal, and supplied numberless common interests to classes whose callings formerly kept them far apart. The universal vogue of sport has played its part. When every other man in the country is at once a golfer, a baseball and radio fan, and perforce, an automobile mechanic, the bars between classes can no longer be very high.

The mystery of learning, too, is no longer what it was. The average man is at least superficially, if not really, better educated than formerly, and through his newspaper and innumerable magazines and novels, feels himself quite conversant with the progress of the world. If he lacks real learning and culture, he doesn't know it.

*Presidential address, Detroit Academy of Medicine, 1927.

On the other hand, great diversity of interests, a widening of the fields of professional activity, and a very cogent need of much more intensive professional training, have operated, I think, considerably to limit the opportunity and the desire for general learning and culture on the part of very many members of certain of the professions. All of these factors, and some others which will readily enough occur to you, have altered greatly the status of the professional man, and are bringing about a corresponding change in the type of men who select the various professions, and their mode of practicing them.

Of the three professions of which I have spoken, it seems to me that the law has felt these changes least, while the ministry comes next, and medicine has been most affected. With the first two we need not further concern ourselves here, but in the status and the future of medicine we have a very vital interest.

That any glamor or mystery attached to medicine must disappear as it becomes more strictly scientific and as the public becomes constantly better informed, is obvious, and not at all to be deplored, especially as the same spread of information must in the end bring greater appreciation for real scientific attainment, and less respect for commercialism and pretense. Neither, I think, should we regret the loss of professional dignity and aloofness which has come with the great increase in the number and kind of human contacts and relationships.

I do regret, however, certain changes within the profession itself, some of which I know to be inevitable, others capable of amelioration, at least, and still others perhaps only a passing phase.

In the first place, it seems to me that with the development of medicine, the road to a comfortable livelihood, with a prospect of considerably more than this in some of the specialties, is more definite and assured for the really capable well-trained young practitioner; consequently, there is more tendency to go into medicine as a way of earning an honorable living, irrespective of any motive of altruism, or any special "call" or natural fitness for the profession. This is bad only in so far as it tends to commercialism, or lowers the average quality of the men who enter the profession. There is a real probability, I think, that ours, as well as the other professions, is likely to be considered more and more in the light of a trade, and to lose, perhaps, some of the prestige that justly belongs to it. Over-exploitation of various mechanical aids to diagnosis and therapy—too often for reasons chiefly commercial—is one of the things which just now seems to aggravate this risk.

Secondly, the constant growth in the number of things which the physician must know in order to qualify himself for practice has lengthened the required period of study beyond that needed for any of the other professions. Obviously, unless the boy who is planning to go into medicine can afford a prolonged outlay of time and money, he will have little opportunity to cultivate the humanities, and such "culture" as he has must come chiefly from his environment at

home, and in whatever educational institution he may select. Just how much broad culture may contribute to success in ordinary practice is somewhat questionable. It certainly adds much to the influence of the teacher; and has been a predominant characteristic of a great proportion of the leaders of the profession, and its supposed possession by medical men has had, as I have intimated, much to do with the prestige which they have enjoyed among the laity.

Broad culture, which in itself almost connotes breadth of vision, and high professional ideals, are two things which are in danger of being lost sight of in current medical education, and as they become less distinguishing characteristics of the profession, its prestige is sure to suffer. So far as general culture is concerned, I see no immediate possibility of providing more time for it, either in the pre-medical course or during the years of medical study, nor do I believe that the requirement of the bachelor's degree, which supposes a somewhat broader education, can wisely be made general, though it probably does bring to those schools that do require it a somewhat better class of students. Fortunately, the man with a well-trained mind is perfectly capable of acquiring his general culture in post-academic years, if he feels the need of it. Respect and desire for culture come largely from environment. The boy who comes from a cultured family absorbs not only a respect for it but a very considerable amount of real culture in his early years, which he is not likely ever to lose. The environment of a great university has much to do with inculcating respect and desire for it, even in the professional student who is not there primarily for that purpose. The lack of such environment is to my mind one of the objections to the medical school located in the heart of a big city, and quite separate from the university environment.

High ideals are very largely the result of environment. Early training is a most potent factor, but its effect may easily be lost by unfortunate example in later years. To my mind perhaps the best service of some of the great teachers of medicine has been their constant inculcation, by precept and example, of the highest kind of professional and scientific ideals. To men of this type, and their widespread influence wherever their pupils have gone, more than to any especial excellence of scientific teaching, has been due the preëminence of some of our great schools. Increasing stress on these things is needed if the trend to commercialism is to be successfully held in check.

To my mind the routine problems of medical education—the various questions involved in the endeavor to give the future practitioners the most adequate scientific training within a reasonable period of time—belong strictly to the teachers themselves, and we as practitioners are not so greatly involved in this solution, though we have our part, and an important one, to play, all those of us who have hospital connections, in making the final teaching of the interne years as complete and valuable as we can. A more vital concern for us who re-

spect and love our profession is to see that its dignity and prestige are maintained in the face of the rising tide of commercialism. If I were obliged to make suggestions as to what is particularly needed in medical education, I think I should say that, under present day conditions it would better begin by a careful selection of candidates from the standpoint of character as well as from that of early education and mental capacity. In saying this, I am not implying that the character of the average medical student is low, but thinking of the probability that the tendency toward a lowering of professional standards is likely to increase.

Assuming a selection of students on this basis, I should like further to see more emphasis laid on high ethical standards and professional ideals throughout the training period. Here, of course, the example of the right kind of teachers is of the greatest value, but I think that there might be something more than this, in the way of conscious deliberate effort to implant and foster such ideals, than is now made in most schools. I think, too, that more might be done to the good of the profession to stimulate in the student a desire for as high a degree of general culture as possible. This, as I have said, can hardly be a matter of the required curriculum, but I can think of more than one other means, especially in the campuses of the great universities, if it be made a matter of serious effort.

Editorial

GENERALIZED XANTHOMATOSIS

Rowland (Archives of Internal Medicine, November, 1928) makes an important contribution to our knowledge of xanthomatosis in the correlation of a group of cases described as defects in membranous bones, exophthalmos and diabetes insipidus (Christian's syndrome). He considers fourteen cases all occurring in early childhood, six of the patients being girls and eight boys. In ten of the cases the probable onset of the affection occurred during the second year of life, with one each in the third, fourth, sixth and seventh year. In all cases the onset was insidious and periodic, so that in most cases the disease was well advanced before a physician is called. The family history was negative in all cases save one in which the mother had hypercholesterinemia. Obstetric histories were normal. During the first year, nutritional disturbances did not occur, and development was normal. The blood Wassermann was negative, and tuberculosis was not present. One of the common infections of the age antedated the onset in most instances. In three cases a history of trauma was associated with some of the bone defects. The symptoms depended on the location of the lesions, the extent of involvement and the mechanical effects resulting from pressure and bone destruction. There was a notable lack of subjective symptoms, but during the active stage there was frequently increased irritability, and often tenderness and pain referred to the lesions. The most notable clinical feature was the occurrence of diabetes insipidus in all of the series except two. Glycosuria was found in one case only. Retardation in growth was apparent in most instances from the onset of symptoms. In two cases besides dwarfism, a typical dystrophia adiposogenitalis developed. The varying degrees of exophthalmos which occurred in every case may be explained by the destructive bone process. The fundi in every patient examined were normal. Lesions of the skin suggesting xanthoma were not found in any one of the cases. Lipemia was not observed in any instance; there was usually a slight degree of anemia with a moderate increase of leukocytes. In one case the blood changes were so marked as to lead at first to a diagnosis of anemia pseudoleukemia infantum. Evidences of blood destruction were not found in the case, but the severe anemia was due to the hyperplastic process in the long bones interfering with blood formation. Four of the group came to autopsy. In all the fatal cases there was an extreme degree of pulmonary fibrosis with lipoidosis of the newformed tissue. There have been seven deaths in all, and as far as known

seven of the cases are still living. Two have shown a marked improvement. There should be no difficulty in the clinical diagnosis of the syndrome. In the case of bone defects, especially of the cranium, polyuria, polydipsia, exophthalmos, loosening of the teeth, dwarfism and adiopogenitalis this condition of disturbed lipoid metabolism should be considered. In this connection it is important to remember that the blood serum does not always show an increase in lipoids, and that various lipoids are concerned in the process. The pathologic findings show constantly nodular or diffuse lesions that have a yellowish to yellowish-brown color, appearing to arise from the connective tissue of the dura, periosteum, peritoneum and pleura, and more rarely in the interstitial tissue of certain of the viscera. Histologic examination shows that they were characterized by the presence of great numbers of lipoid-containing cells showing great variability in structure. In some areas they present the appearances of a fibroma, in others of a granuloma, in others they show an angiomatous character; frequently the picture resembles that of a giant cell tumor or sarcoma. They are, however, not true neoplasms; their distribution is not suggestive of a hematogenous metastasis, they lack any infiltrative growth; and their long continued development, symmetrical distribution, and occasional retrogression indicate a systemic growth rather than an autonomous new growth. Rowland regards these nodular growths as arising from the proliferation of the reticuloendothelial system following an excess of lipoids in the blood. One is not dealing with true neoplasms but with lipoid-storage tumors or granulomas. The formation of the nodules is a compensatory act on the part of the body in its attempt to rid the blood of an excess of lipoid which cannot be properly excreted. These views are confirmed by the experimentation of Anitschkow and Kuczyuski, and by the studies of microscopic changes by Wustman, Weber and others; and are of great clinical interest in that they bring into relationship with this pathogenesis a long series of xanthomatous new formations arising from the dura, periosteum, pleura, pericardium, peritoneum, endosteum, and from the tendinous, peritendinous and periarticular surface and fascia. The nodular xanthomatous lesions are the result of perpetual blockage. The histiocytes, being immediately filled by lipoids from the body fluids, become refractory to all other substances and so stimulate the demand for new cells, which in their turn become loaded and repeat the process provoking the continuous increase in the new formation. The xanthoma nodule does not increase by the multiplication of its lipoid cell elements, but by the addition of new histiocytes. The bone-destruction associated with these nodular lesions constitutes a notable clinical feature of the affection. In every instance the cranial bones have suffered most, but the x-ray studies have demonstrated similar, though less extensive, defects in the flat bones of the pelvis, more rarely in the scapulæ, ribs and vertebræ, and in one instance in the humerus and femur. Usually thickening or evidence of bone regeneration was not found. The bony

structure adjacent to the defect appeared normal. The frequent presence of foreign-body giant cells in the lesions, in association with pressure, sugguests the explanation for the bone destruction. An early symptom observed in the majority of the cases was an irritated condition of the gums, with loosening of the teeth. The teeth themselves appeared normal, except for erosion of some of the cusps. This condition resulted from xanthoma nodules arising from the periosteum covering the maxillary bones. There were many foreign-body giant cells in these tumor-like xanthoma masses with the same bone destruction present. As to the occurrence of diabetes insipidus it is possible that xanthomatous lesions found at the base of the skull, surrounding the hypophysis and occasionally involving the posterior lobe of the pituitary body, may through pressure or irritation be the cause of the diabetes insipidus, or there may be primary lesions in the hypophysis. Christian and Schüler regarded the syndrome as probably due to a primary disturbance of pituitary function; and various other observers explain disturbances of lipoid metabolism as the result of disturbed function of certain endocrine glands. Rowland believes that the metabolic disturbance is primary, and that the evidences of disturbed hormone action on the part of the endocrine is the result of the pressure of the xanthomatous reticulo-endothelial hyperplasia in these glands. The special service rendered by Rowland in this extensive study of his on the syndrome "defects in membranous bones, exophthalmos, and diabetes insipidus," lies in his correlation of the many forms of localized or generalized visceral xanthomatoses of the reticulo-endothelial system, under the conception of a lipoid metabolic disease of the reticulo-endothelial system—a *lipoid gout*. On the one hand are the yellow to yellowish-brown lipoid-containing xanthomas, endotheliomas, angiomas, giant cell tumors, and giant cell fibrosarcomas of the periosteum, fascia, tendon-sheaths, peritoneum and pleura, skin, etc., that are not autonomous new growths but represent lipoid-storage tumors. On the other hand, Niemann's disease is the rapidly developing xanthoma of infancy, while Gaucher's disease represents a similar condition with an infiltration of more complex lipoproteins, and the various generalized xanthomatous deposits associated with diabetes mellitus or glycosuria, icterus and certain affections of liver or kidneys—all represent primary disturbances of lipoid metabolism. Each of these conditions differs in clinical form, in the pathologic structure of the lesions and in the nature of the lipoids concerned; but they all represent the same irritative proliferation of connective tissue elements—reticulo-endothelial hyperplasia; in other words, there is no essential difference between Niemann's disease, Gaucher's disease, Christian's syndrome, and the many forms of xanthoma. They are all manifestations of the same pathologic process, modified by certain differences in the patient's general metabolic state. The recognition of the fact that underneath all of this varied symptomatology there is a *hyperlipoidemia* is of the greatest importance in suggesting the methods of treatment to be followed.

Abstracts

Klinische and Experimentelle Beiträge zur Frage der Hodentransplantation. By Dr. L. Schönbauer and Dr. F. Hogenauer (Archiv f. Klinische Chirurgie, May 15, 1928).

In the literature of the last several years the question of the transplantation of the testis has received much attention, and the effects of auto-, homo-, and heterotransplantation have been extensively studied. The experimental investigations of Voronoff and their clinical applications have appeared to open up a new field of work. The question of the rejuvenescence of the senescent organism stands in the foreground of the Voronoff investigations. This observer has developed his own method of operation, which consists essentially in the transplantation of the testis upon the tunica vaginalis. According to Voronoff the testis of a chimpanzee transplanted in this way into a man showed, on histological examination, fifteen months later, preserved epithelial cells in the seminal tubules. Through such testis transplantations Voronoff claims to produce a rejuvenescence both in the case of man and in animals. In his book, "Prevention of Age through Artificial Rejuvenescence," he has described a number of successful operations in man and animals. Other authors have confirmed the rejuvenating effects of testicular transplantation. Max Thorek confirms the value of homo- and heterotransplantation of the testis in 97 cases of his own, and claims to have obtained healing in 31 cases and an essential improvement in 28 cases of senility, defect of testes, neurasthenia, impotency on non-organic basis, and dementia præcox. Homotransplantation succeeded much better than heterotransplantation. Among others reporting similar good results are Hunt, Falcone with the transplantation of sheep's testis, Walker in the case of inguinal testis, Stanley with injection of testicular extract and testis transplantation (testes of cadavers into living men), Lichtenstein in a clinical observation extending over years, Lydston, Mühsam, Pfeiffer, McKenna and others. Opposed to the results and opinions offered by the above workers stands a long series of observations by numerous workers who deny that testis transplantation has any effect upon the organism. Enderlen opposes Voronoff's views on the ground of four cases, in which microscopic examination made several weeks after the transplantation showed only necrosis and fatty degeneration of the transplanted organs. To the same results and the same opposing views come Kreuter, Lexer, Förster, Hamesfahr, Buchhardt and Hilgenberg, Brandt and Lieschied (who attained a transitory result) and Kurtzahn who regarded the effects of the transplantation as due to resorption processes and not due to the action of living cells. Haberlandt has shown in a large series of experiments that every autoplastic transplanted testis undergoes necrosis, no matter by what technical method, or where it is transplanted. The contradictory results offered in the literature led the present workers to study the results of auto- and homotransplantation in Rhesus apes. From their results in 13 cases in which the transplants were examined histologically in serial sections it is shown conclusively that free transplanted testis tissue undergoes necrosis and is absorbed, no matter whether implanted intra- or extraperitoneally or according to the method of Voronoff in the tunica vaginalis. As early as 2½ months after the transplantation the transplanted testes are wholly fibrous and atrophic, and are still recognizable, even after 3 and 5½ months. In the intraperitoneal and extraperitoneal implants in some cases nothing of the testis remains or only scar tissue was found. In one case there was found a completely atrophic testis. It appears striking that in a large number of the experiments no testicular remains could be found at the place of implantation, only scar tissue remained; where a transplant was yet

visible it was reduced to a microscopic remnant. This complete disappearance occurred even in the animals examined at 2½ months. Such a disappearance can only be explained on the ground of an enormously rapid resorption. The occurrence in the preparations of the silk sutures showed that the transplant had actually been taken out of the place in which it had been implanted. Also in the animals with autotransplantation (transplantation of its own testis) the transplant was found to be after 5 months completely transformed into fibrous connective tissue, although here the conditions were of the most favorable character. In addition to these animal experiments Schönbauer and Hogenauer operated upon four human cases according to the method of Voronoff. Of these four cases two permit an invalidated judgment as to the value of the operation, in that one of the patients showed a favorable result although the possibility of this being the result of psychotherapy cannot be denied, making it difficult to regard this case as a successful outcome of the Voronoff operation. The second case showed no change. In the third case the patient felt more capable of work 2½ months after the operation, but showed no further change after this time. The fourth case was complicated by prostatic hypertrophy and a bladder fistula; 3 months after the operation the patient felt more capable of work and there was an increase of libido. On the ground of their experimental investigations and the few clinical observations the authors agree with Enderlen, Haberlandt and Hofmeister that the Voronoff operation, aside from its psychical influences upon the patient, does not fulfill its expectations.

Dissemination of the Broad Tape-Worm by Wild Carnivora. By TEUNIS VERGEER (The Canadian Medical Association Journal, December, 1928, p. 696).

The dog, the fox, and the cat are known to serve as hosts of the adult broad tapeworm of man. Because of family relationships it is safe to assume that the wolf, the coyote, and the lynx are capable of serving as hosts. Since all of these eat fish, they in all probability are factors in the dissemination of broad tapeworm in rgeions where fish are infested with the larva. Bears are common in infested territories and catch and eat fish during the spawning season. Two bears have been experimentally infested with D. latum, and thus the bear has been shown to be a very capable host of the broad tapeworm of man. The abundant bears in infested territories must constitute a considerable reservoir of broad tapeworm. Since they like to be in and about water, their egg-laden droppings must cause considerable reinfestation of the fish. Because wild carnivores disseminate broad tapeworm the infestation of fish with broad tapeworm larvæ cannot be completely controlled by man.

Diabetes Therapie mit Acoin. By DR. BERNHARD VOIGT (Klin. Wochenschr., Sept. 30. 1928).

The preparation "acoin," chemically alkyloxyphenylguanidin, prepared by the firm of Heyden, has been used in the treatment of diabetes by Izar, Cannavo and Scuderi, on account of its guanidin components. They reported that in three cases its use produced a lowering of glycosuria and of acidosis, but without effect on the bloodsugar. Voigt treated nine cases of diabetes with acoin. The drug was given in doses of three tablets three times daily, about 0.45 g. With the exception of the bad taste the drug was well borne. No influence was noted either on the glycosuria or acidosis, nor on the bloodsugar. In some of the cases the acoin was combined with insulin after a stability of the carbohydrate metabolism had been obtained through the treatment with insulin alone. No effect attributable to acoin was seen. On the ground of these experiments the writer concludes that acoin is of no value in the treatment of diabetes.

Ueber die Veränderungen der Niere beim Insulinbehandelten Coma Diabeticum mit Ausgang in Urämie. By E. J. KRAUS and H. SELYE (Klin. Wochenschr., August 26, 1928).

In an article entitled "Coma diabeticum and Insulin," Th. Weiss has during the last year reported on 38 cases of diabetes mellitus, which partly in the precoma and partly in fully developed coma, had been

treated with insulin. Among the cases which died in spite of the insulin treatment were three that after the recovery from the coma developed on the 2nd or 3rd day oliguria and anuria, with increase of blood pressure and nitrogen, with a lowering of the general condition, followed a few days later by death in deep coma, differing from coma diabeticum, chiefly in the manner of respiration. The nitrogen retention and increase in blood pressure, the appearance of albumin and casts in the urine, the anuria, and the development of a comatose condition with appearances of motor irritability, pointed to the kidneys as the cause of the premortal condition. The anatomic-histologic examination of the kidneys in two of the cases showed in one case a hemoglobinuria and in the second a slight fatty change in the renal cortex. On the ground of the morphologic examination Weiss ascribed the death in the three cases to a functional, anatomically not visible, injury to the kidneys, which he believed to be caused by the heavy water, sugar and acetone-body excretion during the coma, leading after the cessation of further damage to an irreparable functional disturbance. Kraus and Selye have had in a short time three analogous cases, in which, wholly in opposition to the observations made by Weiss, there were found severe and characteristic morphologic changes in the kidneys sufficient to explain the clinical picture of uremia. Macroscopically the kidneys in all three of the cases presented a high degree of anemia of the markedly swollen organ, and a yellowish color presumably due to fatty change in the parenchyma and a marked edema. The histologic examination showed a marked edema, an abundant collection of fluid in the lumina of the convoluted tubules and the ascending limb of Henle's loops. In spite of the yellow color no fat was found in 2 of the cases and in the third only a slight fatty change in the renal cortex. The changes in the renal epthelium consisted of cloudy swelling, and of a large drop, hydropic-vacuolar swelling of the convoluted tubules, in two cases in necrosis of some of the epithelium of some tubules, which in the one case of postmortal autolytic changes was difficult to differentiate from the latter changes. Striking was the anemia of the kidneys in all cases, especially in the cortex, and here in the glomeruli. In one case which had suffered from anuria for seven days and in which the renal insufficiency had lasted the longest time a part of the glomeruli showed a little blood in the tufts and a moderate injection of the vessels in the medullary substance. In two cases the endothelium of the glomeruli was more or less swollen and very light colored. No leukocytes were demonstrable within the glomerular tufts. In the third case after long search a few erythrocytes were found in the lumina of single convoluted tubules. In all three cases the distal convoluted tubules were filled with a markedly eosinophile, granular mass. The characteristic deposits of glycogen in diabetes were present in all three cases. The authors believe that in their 3 cases of uremic coma developing after insulin treatment of diabetic coma, they have found characteristic kidney changes which make clear the cases of uremia described by Weiss. They believe that these renal changes represent an *especial form of acute nephritis,* in its earliest stages, the exact cause of which they cannot answer, but which they believe to have a causal relation with the insulin treatment of coma diabeticum. As an expression of the earliest beginnings of nephritis they interpret the marked anemia of the kidney, the serous exudation into the capsular spaces and the tubules, and the regressive changes in the convoluted tubules, and the total failure of cellular exudation. For the nephritic character of the affection in these three cases, speaks with a degree of certainty the increase in the blood-nitrogen, the rise in blood pressure and the clinical picture of uremia. When it is considered that these cases presented signs of renal insufficiency for such a short time, only a few days, it is comprehensible that the histologic changes of an acute nephritis in these cases must be of the very earliest stages. From the cases described by Weiss those of Kraus and Selye are distinguished by the immediate development of uremia after the diabetic coma, while in those of the former author a period of relatively well-being existed between the diabetic coma and the uremia.

Reviews

The Peaks of Medical History. An Outline of the Evolution of Medicine for the Use of Medical Students and Practitioners. By CHARLES L. DANA, A.M., M.D., LL.D., Professor of Nervous Diseases, Cornell University Medical College, Late President of the New York Academy of Medicine, etc. 105 pages, 40 full-page plates and 16 text illustrations. Second Edition. Paul B. Hoeber, Inc., New York, 1928. Price in cloth, $3.00.

The first edition of this work appeared in April, 1926, and the fact that a second edition is called for within so short a time must be encouraging both to the author and his editor. No especial change has been made in this second edition. A few illustrations have been added, and some practical criticisms involving minor slips in the wording of a legend, or some inaccuracy in typography have been carefully attended to. Comments on the work, so far made, have been mostly those of approval. The object of this short history of medicine has been, as we pointed out in our review of the first edition, the presentation chronologically of the main facts of the evolution of medicine from pre-Hippocratic times, down to the middle of the nineteenth century, giving a rapid survey of the special movements marking the progress of medical science. The high spots, or peaks in the evolution of medicine are so emphasized that the student can in a short time obtain a visualization of the subject as a whole, and in this way acquire a background upon which he can work out details in accordance with his interests and tastes. Six peaks, that of Hippocrates, the Alexandrian School, Galen, the Renaissance, Harvey and Jenner mark the seven periods into which the history of medicine naturally falls. These peaks are shown in a diagram on the first page. After a brief opening chapter on ancient medicine there follow six main chapters of exposition according to this diagram, and these in turn are followed by a chapter of bibliographical notes on books to be read by the student in his further studies in medical history. The illustrations form an especial feature of the book, in that they are *kinetic* rather than static in character, and intended to give social atmosphere to a text which is preponderately biographical. We can only repeat here what we said of the first edition. The material used in the text is excellently chosen, and presented in an agreeable readable manner. The book fulfills its aims in a high degree of excellence. It is beautifully printed, the illustrations are excellent, and the full page printings of the Oath o fthe Hindu Physician and the Oath of Hippocrates add to the general impression of fine workmanship which the book gives as a whole. We recommend this work highly, both to students and to practitioners, in that it offers a systematic presentation of the high spots in medical history.

The Clinical Examination of the Nervous System. By G. H. MONRAD-KROHN, M.D., F.R.C.P., Professor of Medicine in the Royal Frederick University, Oslo; Physician-in-Chief to the Neurological Section of the State Hospital, Oslo; Also in Charge of the Hospital's Out-Patient Department for Nervous and Mental Diseases; Corresponding Member of the Neurological Societies of Paris, Copenhagen, and Estonia. With a Foreword by T. GRAINGER STEWART, M.D., F.R.C.P., Physician to the National Hospital for the Paralyzed and Epileptic, Queen Square; Neurologist to the West London Hospital; Physician to the Central London Ophthalmic Hospital; Consulting Neurologist, The Queen's Hospital, Sidcup, and Queen Mary's Hospital, Roehampton, Corresponding Member of the Neurological

Society of Paris. Fourth Edition. 209 pages, 55 illustrations. Paul B. Hoeber, Inc., New York, 1928. Price in cloth, $2.50.

This book is not a translation, but has been written in English by Dr. Monrad-Krohn himself. Hence the book is free from that vagueness of meaning which is common to so many translations. If at times the author's mode of expression may strike the reader as unfamiliar, he always succeeds in making his meaning clear and in emphasizing his point. The third English edition was printed in 1926, and its continued success has necessitated the publishing of this fourth edition. In this book the author describes a routine method of examination of the nervous system which he has adopted in his neurological clinic, and has given an outline of the clinical tests which he himself considers to be the most practical and useful. He has shown an appreciation of the true needs of the neurologist and psychiatrist in that he had not confined his book to the purely neurological aspects of nervous disease, but includes an outline of the examination of the mental state of the patient. He insists upon the importance of combining a knowledge of neurology with that of psychiatry. He further emphasizes the fact that proficiency in neurological examination can only be obtained through practice, and that his book is intended for use in close connection with clinical work. For the present edition he has again revised the book, making some minor additions and alterations. In the choice and description of the various methods the author has been guided by experience gained in the daily work in his clinic. A short chapter on the interpretation of x-ray pictures of the skull has been added, which gives a few points which according to his experience, both the beginner and the practitioner are apt to overlook or to misinterpret. The contents include the: Anamnesis; the Status Præsens, including the mental state, the cranial nerves, motor system, associated movements, coördination and cerebellar signs; the sensory system, including superficial sensation, deep sensation, combined sensation, sensory paths and segmentation; the reflexes, including the deep reflexes, cutaneous reflexes, reflexes of spinal automatism, postural reflexes, organic reflexes, and reflex formulæ; the standing position; the gait; simulation; electrical examination; the examination of cerebrospinal fluid, and puncture of cisterna magna. The main method of routine neurological examination is then followed by appendices on the Binet-Simon tests, psychosomatic examination, diplopia, vestibular tests, anatomical diagrams, pharmacological tests of the vegetative nervous system, the interpretation of x-ray photographs of the skull; on repeated examinations and on the first routine examination. All in all, this book represents the most complete and best abridged method for the clinical examination of the nervous system that has yet been published. It has been brought thoroughly into line with the results of recent medical research. Of especial practical importance is the author's emphasis of the fact that the neurological examination without an adequate investigation of the patient's mental condition is incomplete, and that the psychiatric examination is equally incomplete unless accompanied by a complete neurological examination. The author gives wise advice to medical students in the following procedure of examination: "First, complete the systematic examination; give the examination your whole attention without speculating about the diagnosis until the examination has been completed. Then write out a tabulated list of your findings; it is most convenient to arrange them in two columns corresponding to the two sides, Right and Left. Next, try to arrive at a *focal diagnosis* based on your anatomical and physiological knowledge. Finally, consider the *nature* of the lesion, aided by your knowledge of general pathology." We recommend this little book most warmly as a guide to neurological examination.

Roentgenology. Its Early History, Some Basic Physical Principles and the Protective Measures. By G. W. Kaye, O.B.E., M.A., D.Sc., F.Int.P. 157 pages, 49 illustrations. Paul B. Hoeber, Inc., New York, 1928. Price in cloth, $2.00.

This monograph represents an expansion of the author's Caldwell lecture, given in 1927, before the American Roentgen Ray Society's meeting in Montreal. It is a reprint with additions, from the American Journal of Roentgenology and Radium Therapy, Volume XVIII, No. 5, November, 1927. In the present volume, the earlier chapters particularly, which touch on certain historical and physical aspects of roentgen-rays have been enlarged and expanded by various additional material. The later chapters have been written particularly for hospital authorities who seek to improve the working conditions in their roentgen-ray departments. The opportunity has been taken to include the International Recommendations for X-Ray and Radium Protection which were adopted at the Second International Congress of Radiology held in Stockholm, in July, 1928. The ten chapters of the book are given up to: I, Some Early Philosophers; II, The Nature of Roentgen Rays; III, Total Reflection of Roentgen Rays; IV, Prismatic Refraction of Roentgen Rays; V, Diffraction of Roentgen Rays by Ruled Gratings; VI, The Nature of Radiation; VII, Roentgen-Ray Protection; VIII, Measurement of Protective Values; IX, Working Conditions in Roentgenographic Departments; X, The Future of Roentgenology. These are followed by the References and Appendices A and B. Of particular interest are the illustrations, many of which are reproductions of interesting old prints, showing early scientific experiments in the attempt to produce a vacuum, and the production of electric discharges *in vacuo*. Hauksbee, about 1705, was the first to conduct experiments along the latter line. In 1740, the Abbé Nollet, devised the "electric egg," which was not an unsuitable term for the prototype of the roentgen-ray bulb. It was Morgan, who in 1785, was able to obtain so good a vacuum that an electric discharge was prevented from passing, and who probably was the first to generate x-rays, had he but known it. By the end of the 18th century the electric discharge tube was an established fact. Progress was more rapid during the 19th century, when Davy, Faraday, Geissler, Plücker, Hittorf, Crookes, Lenard and other noted workers brought the line of development up to 1895 and the discovery by Roentgen of x-rays, when the science of radiology or roentgenology was brought into being. The subsequent history of the development of radiology is told in a discussion of the chief features in the next several chapters. The remaining portion of the book is given up to a consideration of roentgen-ray protection, protective values and the working-room conditions of x-ray departments. Aside from the interest of the historical sketch of the scientific experiments leading up to and preceding the discovery of x-rays, the book has a practical value in the soundness of the principles of protection advocated. It may be recommended to any student interested in roentgenology.

College News Notes

PROGRAM
THIRTEENTH ANNUAL CLINICAL SESSION

BOSTON COMMITTEES

JAMES H. MEANS, *General Chairman*

COMMITTEE ON ARRANGEMENTS

JAMES H. MEANS
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COMMITTEE ON HALL

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PRELIMINARY PROGRAM
ANNUAL CLINICAL SESSION
THE AMERICAN COLLEGE OF PHYSICIANS
APRIL 8-12, 1929

Monday, April 8, 1929

OPENING SESSION, 2:30 O'CLOCK

Hotel Statler Ballroom

1. Addresses of Welcome. David L. Edsall, Dean of Harvard Medical School. Alexander S. Begg, Dean of Boston University Medical School. A. Warren Stearns, Dean of Tufts College Medical School. John M. Birnie, President of Massachusetts Medical Society. Lincoln Davis, President of Suffolk District Medical Society.

2. Reply to Addresses of Welcome. Charles F. Martin, President of The American College of Physicians.

3. Tuberculosis: A Confession of Faith. Lawrason Brown, Saranac Lake, N. Y.

4. (Title not yet announced.) Lewellys F. Barker, Baltimore.

5. Juvenile Diabetes. I. M. Rabinowitch, Montreal.

6. Glycosuria. James E. Paullin, Atlanta.

7. Clinical Aspects of Paroxysmal Hypertension. M. C. Pincoffs, Baltimore.

EVENING SESSION, 8:00 O'CLOCK
Hotel Statler Ballroom

Symposium on Deficiency Diseases

1. The Fundamental Nature of Deficiencies. George R. Minot, Boston.

2. Pathology of Deficiencies. S. Burt Wolbach, Boston.

3. Biochemistry and Physiology of Deficiencies. George R. Cowgill, New Haven.

4. Pellagra. Joseph Goldberger, Washington, D. C.

5. Pernicious Anemia. Randolph West, New York.

Tuesday, April 9, 1929
MORNING, 9:00 TO 12:00 O'CLOCK
Hospital Clinics

AFTERNOON, 2:30 TO 5:00 O'CLOCK
Hotel Statler Ballroom

1. Fatigue and Infection. W. L. Holman, Toronto.

2. Neoplasms. J. B. Murphy, New York.

3. Specific Dynamic Action of Protein, Fat and Carbohydrate in Altered States of Nutrition. Edward H. Mason, Montreal.

4. The Relation of Neisserian Infection to the Various Types of Arthritis. O. H. Perry Pepper, Philadelphia.

5. The Fallacy of Vaccine Therapy. Charles C. Bass, New Orleans.

6. The Treatment of Angina Pectoris. Harlow Brooks, New York.

7. The Coronary Problem. Arthur R. Elliott, Chicago.

8. Clinical Aspects of Trichiniasis. Lewis A. Conner, New York.

9. An Intensive Clinical Study of a Graphic Method of Recording Blood Pressure. Louis F. Bishop and Louis F. Bishop, Jr., New York.

EVENING SESSION, 8:00 O'CLOCK
Hotel Statler Ballroom

1. Psychiatry in Relation to Medicine. Austin F. Riggs, Stockbridge, Mass.

2. Syphilis of the Adrenals and Its Relationship to the So-called Idiopathic Addison's Disease. Aldred S. Warthin, Ann Arbor.

3. Lung Syphilis. R. I. Rizer, Minneapolis.

A *smoker* will follow this session.

Wednesday, April 10, 1929
MORNING, 9:00 TO 12:00 O'CLOCK
Hospital Clinics

AFTERNOON, 2:30 O'CLOCK
Hotel Statler Ballroom

1. The Treatment of General Paresis. Harry C. Solomon, Boston.

2. Psychiatry's Part in Preventive Medicine. Arthur H. Ruggles, Providence.

3. The Need of Emotional Data in the Medical History. John Favill, Chicago.

4. Milder Forms of Coronary Obstruction. James B. Herrick, Chicago.

5. The Failing Heart of Middle Life. David Riesman, Philadelphia.

6. Hypertension. George C. Hale, London, Ont.

7. Undulant Fever in the United States. George Blumer, New Haven.

8. (Title not yet announced.) Robert A. Cooke, New York.

9. Tobacco Smoking and Gastric Symptoms. Irving Gray, Brooklyn.

EVENING SESSION, 8:00 O'CLOCK
Hotel Statler Ballroom

1. Serums and Vaccines in the Prevention and Treatment of Disease. Benjamin White, Boston.

2. Clinico-Roentgenological Conference. M. C. Sosman and Associates, Boston.

Thursday, April 11, 1929
MORNING, 9:00 TO 12:00 O'CLOCK
Hospital Clinics

AFTERNOON, 2:30 O'CLOCK
Hotel Statler Ballroom

1. The Treatment of Acute Asphyxia. Cecil K. Drinker, Boston.

2. The Significance of Abnormal Metabolic Features in the Management of Thyrotoxicosis. Walter W. Palmer, New York.

3. Can or Will the Internist Practice Preventive Medicine? George H. Bigelow, Boston.

4. Factors in the Prognosis of High Blood Pressure. W. W. Herrick, New York.

5. The Carotid Sinus Reflex (Hering); Its Use in the Diagnosis and Treatment of Certain Cardiovascular Diseases. C. Saul Danzer, Brooklyn.

6. Lead Poisoning from Snuff. Raymond J. Reitzel, Galveston.

The General Business Meeting of The College will be held at 4:00 in the Hotel Statler Ballroom. All Masters and Fellows should attend.

EVENING, 7:00 O'CLOCK

Annual Banquet of The College
To be followed by a Dance.

Address: George E. Vincent, President of Rockefeller Foundation.

Friday, April 12, 1929
MORNING, 9:00 TO 12:00 O'CLOCK
Hospital Clinics

AFTERNOON, 2:30 O'CLOCK
Hotel Statler Ballroom

1. Motion Picture: Demonstrating Its Value in Teaching Electrocardiographic Interpretations of Cardiac Arrythmias. Joseph B. Wolffe, Philadelphia.

2. Dr. William Dunlop and Pioneer Canadian Medicine. J. W. Crane, London, Ont.

3. Rheumatic Fever. Homer F. Swift, New York.

4. (Title not yet announced.) J. C. Meakins, Montreal.

5. Results to Be Expected in Malignant Disease Treated by Radiotherapy. George E. Pfahler, Philadelphia.

6. The Problem of the Nervous Patient. Charles H. Nielson, St. Louis.

7. Endogenous Obesity—A Misconception. L. H. Newburgh and M. W. Johnston, Ann Arbor.

EVENING SESSION, 8:00 O'CLOCK
Hotel Statler Ballroom
Convocation Exercises

The General Profession is cordially invited. No special admission tickets are required.

1. Convocation Ceremony.

2. President's Address. Charles F. Martin, Montreal.

PRELIMINARY PROGRAM OF SPECIAL CLINICS AND DEMONSTRATIONS

This year the general session will be held in the afternoons and evenings, while clinics and demonstrations will be held in the mornings from 9:00 to 12:00.

Special Admission Cards required. Clinic reservation forms and full directions will accompany the Final Program. Reservations may be made by mail or daily at the Registration Bureau.

Special clinics and demonstrations will be held as follows:

A

BETH ISRAEL HOSPITAL

Program in charge of Herrman L. Blumgart

B BOSTON CITY HOSPITAL

1. (A guest will give a clinic at this time; the name will be announced later.)

2. The Progress of the Boston City Hospital. John J. Dowling, Superintendent.

3. Treatment of Pneumonia. Demonstration of Cases. Edwin A. Locke.

4. Clinic of Unusual Cases. Francis W. Palfrey.

5. Pernicious Anemia. Demonstration of Cases. William B. Castle.

6. Treatment of Anemias. Demonstration of Cases. George R. Minot.

WEDNESDAY, APRIL 10, 1929

1. (A guest will give a clinic at this time; the name will be announced later.)

2. Gastro-Intestinal Cases. Franklin W. White.

3. Cardiac Cases. William H. Robey.

4. Nephritis Cases. William R. Ohler.

5. The Surgical Treatment of Pulmonary Tuberculosis. Demonstration of Cases. Edward D. Churchill.

Hypertension and Arteriosclerosis. Demonstration of Cases. Soma Weiss.

THURSDAY, APRIL 11, 1929

1. Cardiac Cases. Edward N. Libby and Thomas J. O'Brien.

2. A Case Illustrating the Value of the Electrocardiogram. James M. Faulkner.

3. Epilepsy. William G. Lennox.

4. Diseases of the Coronary Vessels. Demonstration of Cases. Joseph T. Wearn.

5. Peptic Ulcer. Demonstration of Cases. Maurice Fremont-Smith.

6. Neurological Cases. Stanley Cobb.

7. (A guest will give a clinic at this time; the name will be announced later.)

FRIDAY, APRIL 12, 1929

1. (A guest will give a clinic at this time; the name will be announced later.)

2. Cases of Disease of the Hemopoietic System. Ralph C. Larrabee.

3. Lymphoblastoma. Demonstration of Cases. Henry Jackson, Jr.

4. Tropical Diseases. Demonstration of Cases. George C. Shattuck.

5. Fluoroscopic Diagnosis in Chest Conditions. Demonstration of Cases. Harold W. Dana.

6. Carcinoma of the Head of the Pancreas. Demonstration of Cases. Irving J. Walker.

C BOSTON CITY HOSPITAL
THORNDIKE MEMORIAL LABORATORY

WEDNESDAY AND THURSDAY
APRIL 10 AND 11
BETWEEN 10:30 AND 12:30

Demonstration of Researches Concerning the Following Topics

Dr. Castle and Associates.....Anemia
Dr. Jackson and Associates.....Malignant Tumors
Dr. Lawrence and Associates.....The Physiology and Pathology of White Cells
Dr. Lennox .....Epilepsy
Dr. Minot and Associates.....The Blood
Dr. Nye and Associates.....Bacteriological Problems
Dr. Wearn and Associates.....The Capillaries
Dr. Weiss and Associates.....Vascular Problems

BOSTON CITY HOSPITAL
SOUTH DEPARTMENT

Program in charge of Edwin H. Place

Ward visits on (1) diphtheria, (2) scarlet fever, (3) a few of the other minor groups such as chicken pox, mumps, measles and whooping cough.

Amphitheater demonstration of cases of chronic laryngeal injury and other damages resulting from contagious diseases.

E

BOSTON DISPENSARY

TUESDAY, APRIL 9, 1929

1. Heart Disease. David Davis.
2. Essential Hypertonia. David Ayman.
3. Neurological Clinic. A. Warren Stearns.
4. Obesity. Mark Falcon-Lesses.
5. Gastro-Intestinal Clinic. Percy B. Davidson.

WEDNESDAY, APRIL 10, 1929

1. Bronchiectasis. William Dameshek.
2. Psychalgia. Joseph H. Pratt.
3. Arthritis. John D. Adams.
4. Chronic Pancreatic Disease. Bert B. Hershenson.
5. Tuberculosis. H. Louis Kramer.

THURSDAY, APRIL 11, 1929

1. Neurosyphilis. Arthur Beck.
2. Neurasthenia. Joseph H. Kaplan.
3. Nephrosis. Tobert W. Buck.
4. Domiciliary Medicine in Clinical Teaching—Selected Case. Osadore Olef.
5. Domiciliary Medicine in Clinical Teaching—Selected Case. Charles Korb.
6. Diabetes. James H. Townsend.

F

CHILDREN'S HOSPITAL

Program in charge of Kenneth D. Blackfan

G

HOMEOPATHIC HOSPITAL
EVANS MEMORIAL CLINIC

TUESDAY, APRIL 9, 1929

1. Sterility Clinic. Special Emphasis to be Placed on the Constitutional Factors in Sterility. S. R. Meaker and A. W. Rowe.

WEDNESDAY, APRIL 10, 1929

Endocrine Clinic

1. Endocrine Diagnosis and Therapy. Charles H. Lawrence.
2. Endocrine Disorders Associated with Otosclerosis and the Menière Syndrome. D. W. Drury.
3. Eye Findings in Endocrine Disorders. W. D. Rowland.
4. Cases Presenting Outward Evidence of Endocrine Disorders Found on Study not to have Endocrine Disturbance. A. W. Rowe.
5. Dementia Praecox. L. G. Hoskins.
6. The Follicular Hormone. J. C. Janney.
7. Discussion on Sugar Metabolism as Influenced by Insulin in Pituitary Disease. H. Ulrich and A. W. Rowe.

THURSDAY, APRIL 11, 1929

General Medical Clinic

1. Heart Clinic. W. D. Reid.
2. Intestinal Migraine. C. W. McClure.
3. Neurology. N. H. Garrick.
4. Lung Abscess, Diagnosis and Treatment: Bronchoscopy, the Use of the Bronchoscope in Diagnosis and Treatment. L. R. Johnson.

FRIDAY, APRIL 12, 1929

(Program to be announced later.)

H MASSACHUSETTS GENERAL HOSPITAL

1. Clinic by James E. Paullin, Atlanta.
2. Thoracic Clinic. Frederick T. Lord.
3. Cases of Hypertension. William B. Breed.
4. Cardiac Clinic. Howard B. Sprague.
5. Endocrine Clinic. Walter Bauer and Dwight L. Sisco.

WEDNESDAY, APRIL 10, 1929

1. Clinic by Lewellys F. Barker, Baltimore.
2. Demonstration of Medical Cases. William B. Robbins.
3. Pediatric Clinic. Fritz B. Talbot and Harold L. Higgins.
4. Clinico-pathological conference. Richard C. Cabot and Tracy B. Mallory.
5. Diabetic Clinic. Roy R. Wheeler.

THURSDAY, APRIL 11, 1929

1. Clinic by O. H. Perry Pepper, Philadelphia.
2. Neurological Clinic. James B. Ayer.
3. Psychotherapy of Gastro-Intestinal Diseases. William Herman.
4. Gastro-Intestinal Clinic. Chester M. Jones.
5. Indications for Splenectomy. Arlie V. Bock.
6. Cases of Pernicious Anemia. Wyman Richardson.

FRIDAY, APRIL 12, 1929

1. Clinic by J. C. Meakins, Montreal.
2. Demonstration of Cases. Gerald Blake.
3. Medical Clinic. James H. Means.
4. Demonstration of Cases. F. Dennette Adams.
5. Anaphylaxis Clinic. Francis M. Rackemann.

I NEW ENGLAND BAPTIST HOSPITAL

Program in charge of Albert A. Hornor

J NEW ENGLAND DEACONESS HOSPITAL

Program in charge of Elliott P. Joslin

1. Carcinoma of the Colon and Colitis from the Surgical Point of View. Daniel F. Jones.
2. Gastro-Intestinal Cases. Sara M. Jordan and Chester Kiefer.
3. Thyroid Cases. Frank H. Lahey.
4. Pedigreed Diabetics. Elliott P. Joslin.
5. Surgery in Diabetics. L. S. McKittrick.
6. The Pathology of Diabetes. Shields Warren.

There will be further additions to this program including clinics by larynologists, ophthalmologists, gynecologists and roentgenologists.

K PETER BENT BRIGHAM HOSPITAL

1. Diagnosis of Certain Forms of Heart Disease. Lewis A. Conner, New York.
2. Chronic Myocardial Disease. Henry A. Christian.
3. Results of Treatment of Duodenal Ulcer. E. S. Emery.
4. Some Considerations on the Relation of Cardio-Renal System to Surgery of the Urinary Organs. William S. Quinby.
5. Bronchoscopy in Lung Disease. Lyman C. Richards.

WEDNESDAY, APRIL 10, 1929

1. Cardiac Disease, the Result of Infectious Processes. James B. Herrick, Chicago.

2. Gallbladder Disease. Channing Frothingham.

3. Bronchial Asthma. I. Chandler Walker.

4. Anemia. William P. Murphy.

5. Thrombophlebitis. John Homans.

THURSDAY, APRIL 11, 1929

1. Mitral Stenosis. David Riesman, Philadelphia.

2. Signs of Persisting Infection in Acute Rheumatic Fever. Clifford L. Derick.

3. Hemorrhagic Nephritis. James P. O'Hare.

4. A Surgeon's Views of the Treatment of Peptic Ulcer. David Cheever.

5. Neurosurgical Conditions. Harvey Cushing.

FRIDAY, APRIL 12, 1929

1. Hypertension. Charles F. Martin, Montreal.

2. Vascular Disease in Diabetes Mellitus. Reginald Fitz.

3. Treatment of Certain Types of Cardiac Arrhythmia. Samuel A. Levine.

4. Treatment of Trifacial Neuralgia. Gilbert Horrax.

5. Diuretics. Henry A. Christian.

L

ROBERT BRECK BRIGHAM HOSPITAL

Program in charge of Louis M. Spears
Clinics on Arthritis

M

UNITED STATES NAVAL HOSPITAL

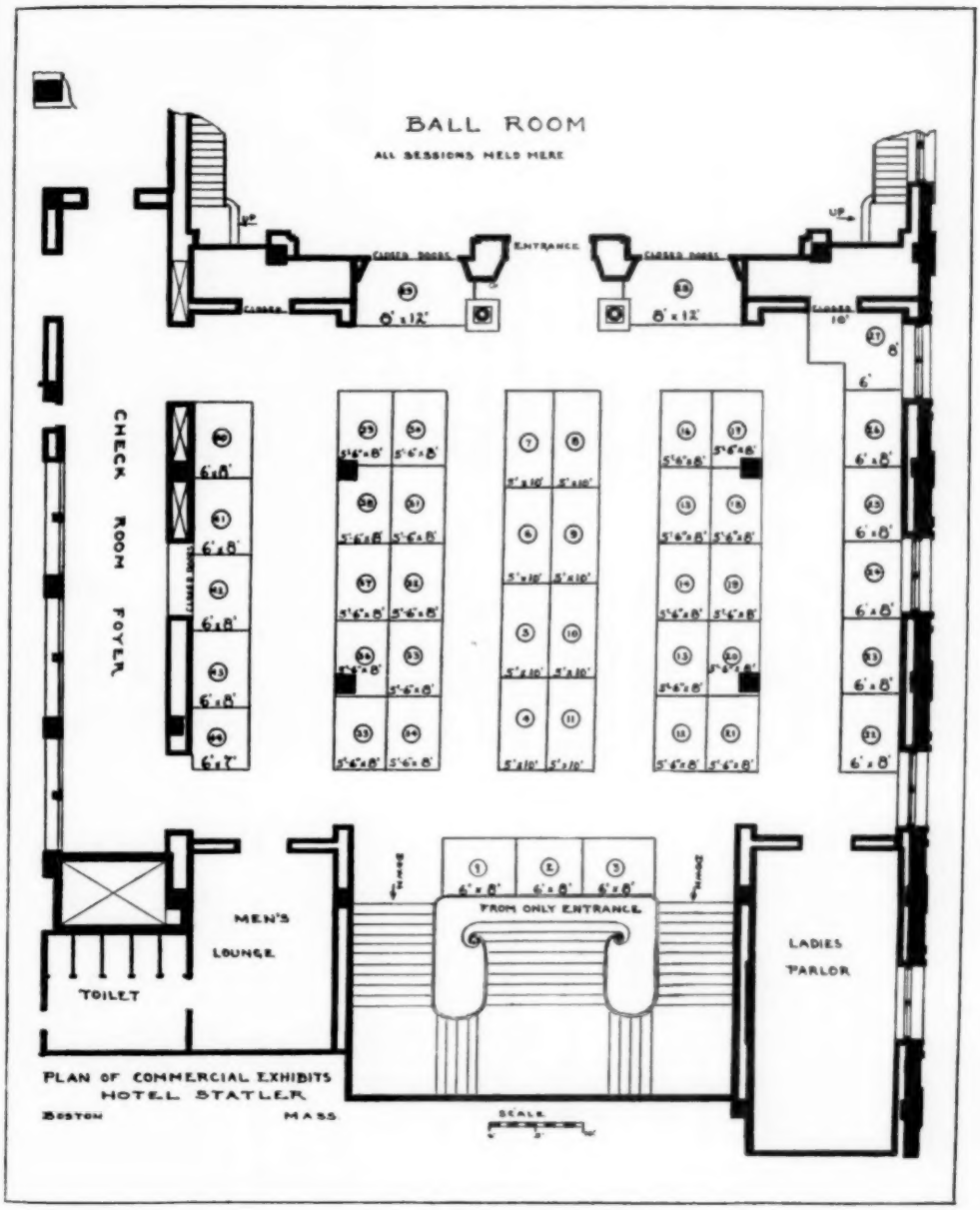
Program in charge of Capt. F. L. Pleadwell, M.C., U. S. N.

Presentation of medical cases in the conference room of the hospital each morning. Following this the group will be split up in sections of five. Each section will be in charge of a ward medical officer, and the balance of the morning will be devoted to ward rounds.

TECHNICAL EXHIBIT

The technical exhibits have been arranged by the Executive Secretary, Mr. E. R. Loveland, and the following chart shows the arrangement of booths and the assignment to exhibitors from various parts of the country. The exhibits are highly diversified in their variety and will bring to the attendants at the Clinical Session, the latest and most improved equipment, the best pharmaceutical products, almost the whole library of medical publications and many other products of special interest to the Internist, Pediatrician, Neurologist, Psychiatrist, Radiologist and research worker.

This Exhibit is undoubtedly the best arranged and the most popular one that The College has yet had. The location is in the Ballroom Foyer where all attendants to the meeting will pass through the exhibits daily. The Joseph T. Griffin Decorating Company, of Louisville, Kentucky, who installed the exhibits for the American Medical Association, the Southern Medical Association and many other prominent medical societies, will be in charge of the booths and decorations.


BALL ROOM
ALL SESSIONS HELD HERE
ENTRANCE
CLOSED DOORS
CLOSED
UP
CHECK ROOM FOYER
MEN'S LOUNGE
TOILET
FROM ONLY ENTRANCE
LADIES PARLOR
PLAN OF COMMERCIAL EXHIBITS
HOTEL STATLER
BOSTON MASS
SCALE

LIST OF EXHIBITORS

Space	Name	City and State	Product
20	Abbott Laboratories	North Chicago, Ill.	Pharmaceutical Products
12 & 21	D. Appleton & Company	New York, N. Y.	Medical Publications
31	The Battle Creek Food Company	Battle Creek, Mich.	Health Foods
22	Bausch & Lomb Optical Co.	Rochester, N. Y.	Microscopes, Photomicro & Projection Apparatus
40	P. Blakiston's Son & Co.	Philadelphia, Pa.	Medical Publications
13	The Borden Sales Company, Inc.	New York, N. Y.	Merrell Soule Infant Foods
26	Britesun, Inc.	Chicago, Ill.	Therapeutic Lamps
25	Cambridge Instrument Co., Inc.	New York, N. Y.	Electrocardiographs & Accessories, and other Physiological Instruments
3	Cameron's Surgical Specialty Co.	Chicago, Ill.	Electro-Diagnostic Surgical & Dental Instruments
44	G. W. Carnrick Co.	Newark, N. J.	Pharmaceutical Products
1	Warren E. Collins, Inc.	Boston, Mass.	Roth-Barach Oxygen Apparatus
14	F. A. Davis Company	Philadelphia, Pa.	Medical Publications
16	Deshell Laboratories, Inc.	Chicago, Ill.	"Petrolagar"
42 & 43	General X-Ray Company	Boston, Mass.	"Morse" Wave Generator, GX-Galvine-Faradie Plate, Diathermy Apparatus, Electrodes
34	Paul B. Hoeber, Inc.	New York, N. Y.	Medical Publications
19	Horlick's Malted Milk Corporation	Racine, Wis.	Malted Milk Products
17	Kalak Water Company, Inc.	New York, N. Y.	Kalak Water
4	Charles B. Knox Gelatine Co., Inc.	Johnstown, N. Y.	Knox Gelatine
15	Lavoris Chemical Company	Minneapolis, Minn.	"Lavoris"
30	Lea & Febiger	Philadelphia, Pa.	Medical Publications
9	J. B. Lippincott Company	Philadelphia, Pa.	Medical Publications

29	MacGregor Instrument Company	Needham, Mass.	Vim Stainless Steel Needles; Vim Emerald Luer Syringes; Vim Surgical & Medical Specialties
8	The Macmillan Company	New York, N. Y.	Medical Publications
2	E. F. Mahady Company	Boston, Mass.	Anaesthetic Apparatus, Laboratory Equipment, Diagnostic & Scientific Apparatus, Vaccines, Intravenous Products, Orthopedic Appliances & Supplies, Instruments for Operating Room, E.F.M. Catgut
18	The Medical Protective Company	Chicago, Ill.	Malpractice Insurance
24	Mellin's Food Company	Boston, Mass.	Mellin's Food
38	Merck & Company, Inc.	Rahway, N. J.	Pharmaceutical Products
23	The Wm. S. Merrell Company	Cincinnati, Ohio	Pharmaceutical Products
32 & 37	Merrell Soule Company	New York, N. Y.	Infant Foods
35	The C. V. Mosby Company	St. Louis, Mo.	Medical Publications
39	Thomas Nelson & Sons	New York, N. Y.	Medical Publications
28	The E. L. Patch Company	Boston, Mass.	Cod Liver Oil
6	Pittsburgh Plate Glass Co.	Pittsburgh, Pa.	"Helioglass"
7	Richards, Inc.	Glenolden, Pa.	Psyllium Seed & Acidophilus Products
11	W. B. Saunders Company	Philadelphia, Pa.	Medical Publications
27	Sanborn Company	Cambridge, Mass.	"Graphic" Metabolism Apparatus
41	Spencer Lens Company	Boston, Mass.	Optical Instruments, Projection Apparatus, Laboratory Equipment
36	Tailby-Nason Company	Boston, Mass.	Cod Liver Oil
5 & 10	Victor X-Ray Corporation	Chicago, Ill.	Electrocardiograph & Quartz Lamps
33	Winthrop Chemical Company, Inc. H. A. Metz Laboratories, Inc.	New York, N. Y.	Pharmaceutical Products

THE WM. S. MERRELL COMPANY

Booth 23

"One hundred years ago, William Stanley Merrell, opened an apothecary shop which was destined to become 'America's Pioneer Pharmaceutical House.' Before the first railroad had been built, when traveling was a tedious and even hazardous undertaking, The Wm. S. Merrell Company had its inception.

"The little retail business grew and prospered. Dr. Merrell was joined in his enterprise by his brother Ashbel and the firm became known as Wm. S. and A. S. Merrell. Later the business developed into a wholesale, importing and manufacturing firm and was incorporated under the name of Wm. S. Merrell and Company."

This is the history of the founding of the name of Wm. S. Merrell Company, an organization that has rapidly grown into one of the foremost pharmaceutical houses in America.

"Definitely associated with the name of Merrell is the pioneer work on the *natural salicylates*. In the present generation, the house has developed the detoxol products, which have contributed a new factor in preventive dentistry; *fibrogen*, the blood coagulant which has already won a place for itself in medicine; and but recently has perfected a new, palatable castor oil emulsion, *lacricin*. That universal household remedy—castor oil—which up to the present time has been esteemed for its medicinal action and abhorred for its taste and odor, has in *lacracin* all the objectionable taste and odor removed, and the full therapeutic potency retained."

KALAK WATER COMPANY

The Kalak Water Company will have an exhibit in the Exhibit Hall—Space No. 17—where Kalak Water will be served, that all physicians visiting the booth may have an opportunity of tasting this highly palatable and agreeable alkaline water.

Kalak Water is made of distilled water and chemically pure salts of the kind normally present in the body, is non-laxative and higher in available alkali and richer in Calcium than any natural or artificial water known.

DASHELL LABORATORIES, INC.

— Petrolagar in Place of Mineral Oil —

The advantages of an emulsified mineral oil over plain liquid petrolatum are so manifest that clinicians everywhere are increasingly adopting Petrolagar for use routinely in the management of intestinal stasis.

Petrolagar is a perfect emulsion of mineral oil with agar-agar, and for convenience is made in four types:

Petrolagar—Plain, No. 1, Blue Label, is the plain emulsion.

Petrolagar, No. 2, Red Label, contains ⅔ of a grain of phenolphthalein to the tablespoonful.

Petrolagar, No. 3, Green Label, is the emulsion combined with 8% milk of magnesia.

Petrolagar, No. 4, Brown Label, is the same as No. 1 except that it contains no sugar.

Petrolagar will be represented by an interesting exhibit at the forthcoming Clinical Session in Boston, Booth 16.

THE BATTLE CREEK FOOD COMPANY

The whole range of Breakfast Cereals, Beverages, Diabetic Foods, Confections, Sanitarium Crackers and Biscuits, new Meat Substitutes, Savita, Food Ferrin, and Food Accessories for Combating Constipation will be exhibited by The Battle Creek Food Company at Booth 31.

"Healthful Living" contains fundamental facts about food and feeding, and may be secured from this Company upon request.

THE BORDEN SALES COMPANY, INC.

At Exhibit Booth No. 13, the Borden Sales Company will exhibit all types of concentrated forms of milk including condensed, evaporated and powdered milk. These will include Merrell-Soule Powdered Whole Lactic Milk, "Klim" and other products.

The Borden Company is today the largest milk concern in the world. This Company, founded nearly three quarters of a century ago by Gail Borden, the inventor of the process for concentrated milk, now handles and distributes every milk product, including fluid milk, condensed milk, evaporated milk, powdered milk, malted milk, ice cream and cheese. Its markets are scattered throughout the world.

LAMOTTE CHEMICAL PRODUCTS COMPANY

The LaMotte Chemical Products Company, Baltimore, Maryland, has engaged an exhibit booth at the entrance to the check room foyer, to be known as Booth No. 45, and entire space will be confined to the showing of LaMotte Blood Chemistry outfits. These offer simplified blood chemistry methods for the general practitioner as well as for the technician, and were developed originally upon specific requests from their patrons. These outfits have become so popular that they have made them available to the medical profession in general. The outfits were developed in co-operation with eminent technicians in institutions where such research is carried on. In each case, the complete apparatus with reagents and complete instructions as as a self contained unit are provided, and at a moderate price. At the Boston Clinical Session, they will exhibit the following:

LaMotte Blood Urea Outfit
LaMotte Blood Sugar Outfit
LaMotte Urine Sugar Outfit
LaMotte Blood Calcium Outfit
LaMotte-Pigford Icterus Index Comparator
LaMotte-Wuth Bromide Comparator
LaMotte Blood pH Comparator
LaMotte Urine pH Comparator

BAUSCH & LOMB OPTICAL COMPANY

Booth No. 22

The emphasis which the World War laid on the medical laboratory, during the years of stress in which it was the scene of intensive research and practice in matters of diagnosis and treatment, developed the laboratory to a point where it is now considered indispensable to hospital practice. It was this emphasis that focused the attention of the American College of Physicians and the American College of Surgeons on the clinical laboratory, which factor is largely responsible for the present constructive interest in it.

A great deal of work coming within the scope of the hospital laboratory involves the use of optical instruments. Tests touching pathology, bacteriology, hematology, serology, immunology, chemistry, etc., and microscopical examinations of urine, blood, frozen sections, cerebra-spinal fluids, secretions and bacteria, require optical equipment of the highest quality and greatest accuracy.

The Bausch & Lomb Optical Company, whose Scientific Bureau has, in many instances, collaborated with such men as Dr. G. Carl Huber of the University of Michigan, Dr. Otto Folin of the Harvard Medical School, and others of like practical experience, are manufacturing a complete line of optical instruments for the medical laboratory. In view of the strides general science has made with the aid of optical instruments, it is fitting that the vast experience of this Company over a period of seventy-five years, through the medium of its products, should be placed at the service of the medical science. The full line of scientific instruments which the Bausch & Lomb Optical Company has especially designed for the medical profession will be on exhibit at Booth 22, Thirteenth Annual Clinical Session of The American College of Physicians, Boston, April 8-12, 1929.

ELECTION TO FELLOWSHIP
BY THE
BOARD OF REGENTS
NOVEMBER 17, 1928

Baldwin, William S.....Lorain, Ohio
Bean, Leo C.....Gallipolis, Ohio
Behlow, Lt. Comdr. William W.....
.....Brooklyn, N. Y.
Bell, Maj. Clarence R....Washington, D. C.
Bierring, Walter L.....Des Moines, Iowa
Blaisdell, Elton.....Portland, Maine
Bloom, Charles J.....New Orleans, La.
Boardman, Walter W.....
.....San Francisco, Calif.
Bogart, Franklin B.....Chattanooga, Tenn.
Breed, William B.....Boston, Mass.
Brereton, Gilbert E.....Dallas, Texas
Brooks, Clyde.....University, Ala.
Carr, B. W.....Washington, D. C.
Chambers, Lt. Comdr. John H.....
.....U. S. S. Mercy, N. Y.
Davis, Arthur E.....Scranton, Pa.
DePew, Evarts V..... San Antonio, Texas
Ferguson, Donald R.....Philadelphia, Pa.
Frank, Lorenz W.....Denver, Colo.
Gasser, Lt. Comdr. Rolland.....
.....Washington, D. C.
Gauss, Harry.....Denver, Colo.
Goldberg, Benjamin.....Chicago, Ill.
Grabfield, G. Philip.....Boston, Mass.
Hall, Harry M.....Wheeling, W. Va.
Hall, Lynn T.....Omaha, Nebr.
Henske, Joseph A.....Omaha, Nebr.
Huston, John.....Ann Arbor, Mich.
Inmon, Capt. Ebner H...Washington, D. C.
Jones, Austin B.....Kansas City, Mo.
Jones, Chester M.....Newton Center, Mass.
Kampmeier, Rudolph H...Ann Arbor, Mich.
Lee, Dee C.....Hot Springs, Ark.
Lee, Roger I.....Boston, Mass.
Lough, Walter G.....New York, N. Y.
McCorkle, Robert G....San Antonio, Texas
Meyer, Julian E.....Columbus, Nebr.
Meza, Ricardo Aquilar....Guatemala, C. A.
Paulonis, Joseph F.....Brooklyn, N. Y.
Pratt, Comdr. Lester L...San Pedro, Calif.
Reifenstein, Benedict W....Syracuse, N. Y.
Riggs, Austen Fox.....Stockbridge, Mass.
Rowland, Whitman.....Memphis, Tenn.
Rupert, Mary P. S.....Philadelphia, Pa.
Sharp, Lt. Comdr. Elwood A.....
.....Pearl Harbor, Hawaii
Shaw, Wm. J.....Rome, Ga.
Sheep, Maj. Wm. L.....Washington, D. C.
Shields, Maj. Wm. S.....Denver, Colo.
Tihen, Henry N.....Wichita, Kansas
Traub, Hugo W.....Chicago, Ill.
Vedder, Lt. Col. Edw. B.....
.....Takoma Park, D. C.
Wallace, Louis O. S.....Kalamazoo, Mich.
Weiss, Soma.....Boston, Mass.
Wesselhoeft, Conrad.....Boston, Mass.
Westhoff, August W. F....Brooklyn, N. Y.
Whitaker, Paul F.....Kinston, N. C.
Wilson, John D.....Scranton, Pa.
Wohlrabe, Arthur A.....Minneapolis, Minn.
Work, Philip W.....Denver, Colo.

EXCERPTS—MEETING OF THE BOARD OF REGENTS
OF THE
AMERICAN COLLEGE OF PHYSICIANS
PHILADELPHIA, PA.

NOVEMBER, 17, 1928

The meeting of the Board of Regents was called to order at The College Headquarters in Philadelphia at 10:30 A. M., Saturday, November 17, 1928, by the President, Dr. Charles F. Martin of Montreal. Those present were: Drs. Aldred Scott Warthin, S. Marx White, John H. Musser, Clement R. Jones, George Morris Piersol, Sydney R. Miller, William Gerry Morgan, George E. Brown, John A. Lichty, Leonard M. Murray, Alfred Stengel, James H. Means, J. C. Meakins, James S. McLester, John Phillips, Charles G. Jennings, President Martin, and the Executive Secretary, Mr. Loveland.

Among guests who were invited to meet with Committees, as members thereof, were the following: Doctors William H. Mercur, Roy R. Snowden, B. A. Cohoe, Maurice Pincoffs, and W. Blair Stewart.

Abstracts of the previous meeting were read by the Executive Secretary, complete Minutes having previously been placed in

the hands of all members of the Board, and upon motion regularly seconded and carried the Minutes were approved as read.

Communications from absent Regents were reported after brief remarks by the President.

The following gifts of publications to the College Library were reported:

By Dr. Edwin Henes, Jr. (Fellow), October 3, 1928: 1925, 1926 and 1927 volumes, Proceedings of the Inter-State Postgraduate Medical Association of North America.

By Dr. Philip B. Matz (Fellow), October 23, 1928: Reprint, "Artificial Pneumothorax in the U. S. Veterans' Bureau."

By Dr. Aaron E. Parsonnet (Fellow), July 3, 1928: Reprint, "Abdominal Manifestations in Cardioascular Diseases." Reprint, "Electrocardiographic Control of Active Digitalization in Auricular Fibrillation." Reprint, "Quinidin Therapy: Uses and Contra-indications in Auricular Fibrillation."

By Dr. M. Lawrence Turner (Fellow), May 1, 1928: Book, "The Life of Pasteur," by Vallery-Radot. Book, "Discovery, The Spirit and Service of Science," by Gregory. Book, "Creative Chemistry," by Slosson. Book, "The Riddle of the Rhine," by Victor Lefebure. Book, "The Future Independence and Progress of American Medicine in the Ages of Chemistry," by and through the Chemical Foundation.

The following resolution was adopted:

RESOLVED, to extend the thanks of the Regents to various donors of gifts, and stress the importance of sending books and literature only that are published by members of The College.

The following deaths were reported:

Dr. Henry G. Brainerd, Los Angeles, Calif. (Fellow); Dr. Joseph Henry Byrne, New York, N. Y. (Fellow); Dr. Ralph Campbell, Los Angeles, Calif. (Fellow); Dr. George P. McNaughton, Detroit, Mich. (Fellow); Dr. S. W. Welch, Montgomery, Ala. (Fellow).

The following resignations, after being individually considered, were accepted, with the recommendation that any who were delinquent at the time of submitting resignation should submit the delinquent dues or be considered dropped from the membership list:

Dr. Wm. J. Carson, Milwaukee, Wis. (Fellow); Dr. Wesley T. Davison, Carmel, Calif. (Fellow); Dr. Louis Bertram Sachs, New York, N. Y. (Fellow); Dr. George Harvey Agnew, Toronto, Ont. (Associate); Dr. W. P. Millspaugh, Los Angeles, Calif. (Associate); Dr. Frank C. Rote, Pittsburgh, Pa. (Associate).

The Executive Secretary reported the offer of a gift of twenty-five hundred books through Colonel Percy M. Ashburn (Fellow), of the Congressional Library, Washington. After liberal discussion, it was decided that inasmuch as The College has limited accommodations for the storing of books and a questionable need for a general library, that it shall be the future policy of The College to accept only publications by members of The College, for those would serve as a valuable directory and possibly a memorial library of the members of this organization.

The Executive Secretary was instructed to send an explanatory letter to Colonel Ashburn, the letter having been prepared by President Martin.

After further discussion, the following resolution was adopted:

RESOLVED, that the only library which this organization is endeavoring to gather shall be composed of publications by its own members.

An invitation from the Pan American Medical Association to attend their next Congress in Havana, December 29 to January 3, was read.

The following Life Membership subscriptions were reported:

Dr. C. F. Martin, Montreal, Quebec, Can.; Dr. Carl R. Comstock, Saratoga Springs, New York.

The following changes in status were reported:

Dr. Roland Davison from M. C., U. S. A. Service, Letterman General Hospital to Medical Director, Desert Sanatorium.

Dr. Russell Pigford from full-time teacher at Tulane to private practice at Tulsa, Okla.

The following resolution was adopted upon motion by Dr. Warthin, seconded by Dr. Stengel:

> RESOLVED, that a copy of Annals of Internal Medicine be sent to the British Museum each month and that no further complimentary subscriptions be entered except upon approval by the Board of Regents.

Dr. Alfred Stengel, Chairman of the Committee on ANNALS OF CLINICAL MEDICINE, submitted a full report dealing with the termination of the former publishing contract with the Williams & Wilkins Company, of Baltimore. The details of his report are printed elsewhere under "College News Notes" (December Number).

Editor Warthin pointed out that it would be desirable for him to index the new volumes of Annals of Internal Medicine under both an old series and a new series number, thus tying in the new journal with the first five volumes of Annals of Clinical Medicine.

Dr. Martin expressed the appreciation of the Regents to Dr. Stengel and his Committee, Dr. Jones, Dr. Barker and Dr. Piersol, for the labor that they have undertaken with regard to the bringing to a successful close the controversy with Williams & Wilkins.

Under new business, the matter of Dr. Mercur and his project for having The American College of Physicians appoint a committee to make a study of Groups and Clinics, with a view to formulating rules whereby The College will officially recognize such groups, was discussed. Dr. Martin reported that Dr. Mercur's Committee, consisting of Dr. Mercur, Dr. B. A. Cohoe, Dr. Sydney R. Miller, Dr. Theodore R. Squier and Dr. R. R. Snowden, had met with a committee of the Board of Regents in which the subject of "Groups and Clinics" had been discussed and a recommendation in the way of a report from Dr. Mercur filed. The plan proposed by Dr. Mercur and his Committee provides that The American College of Physicians shall formulate a set of standards which shall cover groups and clinics and shall initiate a plan whereby The College would accredit or approve those groups and clinics which meet the proposed standardization rules. Dr. Mercur's final request was that the Regents appoint a committee to study further into the question in order that a definite conclusion might be submitted at a later meeting.

Upon motion by Dr. Warthin, seconded by Dr. Stengel and regularly carried, the following resolution was adopted:

> RESOLVED, that a committee shall be formed, consisting of members of the Board of Regents, to thoroughly investigate the recommendations of Dr. Mercur's Committee for accrediting groups and clinics, and report back at the next meeting of the Board of Regents at Boston.

President Martin appointed the following to act on the Committee:

Dr. John H. Musser
Dr. James McLester
Dr. Leonard M. Murray

The Executive Secretary reported that although every effort had been made to collect delinquent dues during the past year, there are still outstanding fifty-three Fellowship dues delinquent for two years and forty-three Associateship dues delinquent for two years. The list of names was submitted to the Board of Regents and President Martin presented a draft of a proposed letter which he recommended be sent to the list. Upon motion by Dr. Warthin, seconded by Dr. Jones and regularly carried, it was resolved that the letter proposed be distributed to all such delinquent members.

Dr. James H. Means, General Chairman of the Thirteenth Annual Clinical Session, reported in full upon the preparations for the Boston Clinical Session in 1929, presenting copy of the program in detail as arranged up to this time.

Dr. Warthin reported that many members have complained of too elementary clinics, and asked that every means be taken to see that speakers on the scientific program have their manuscript ready to hand to the re-

porter at the meeting. The Executive Secretary reported that all speakers are sent a marked program showing when and where they appear and also asking for an advance copy of the manuscript. Dr. Warthin requested that the more important clinics be written up and Dr. Means expressed a willingness to circularize the participants, stating that if they would care to write up their clinics, Dr. Warthin will be glad to consider them for publication in Annals of Internal Medicine.

President Martin expressed the appreciation of the Board to Dr. Means for taking so much care in the preparation of his advance program, and reported that Dr. George Vincent of the Rockefeller Foundation has agreed to be a speaker at the Banquet.

The Executive Secretary, Mr. Loveland, presented his report concerning the new headquarters of The College, the general activities of the business offices, membership activities, business preparations for the Clinical Session, promotion in advertising and circulation of ANNALS OF INTERNAL MEDICINE, and other matters concerning the business administration of The College.

Dr. Warthin recommended that publishing organizations, whose books are reviewed in Annals of International Medicine be placed on the complimentary subscription list of the Journal. He further pointed out the success of his office and the Ann Arbor Press in bringing the Journal out on time and stated that it is his plan now to distribute the Journal on the fifteenth of each month. He expressed dissatisfaction with the advertising of the Smith, Kline and French Company in Annals of Internal Medicine and recommended that only "council approved" pharmaceutical products be accepted. He further suggested that advertising be restricted to sanatoria, publishing houses, instrument companies and manufacturers of "council approved" products.

Dr. Charles G. Jennings, Chairman of the Finance Committee, reported that the Executive Secretary had placed in his hands complete financial data for his Committee's consideration. The Committee's report, after due consideration, was as follows:

"In view of the present financial condition of The College, as reported by the Treasurer and the accounts of the Executive Secretary, and further in consideration of the immediate prospect of the adoption of changes in the Constitution and By-Laws, which will reduce the income from new members, it is deemed inadvisable at the present time to reduce either the initiation fee or the annual dues."

The report of the Committee on Finance was thereafter approved by the Board of Regents.

Dr. Sidney R. Miller, Chairman of the Committee on Constitution and By-Laws, presented mimeographed copies of the suggestions of his Committee. These were read and considered separately with suggested revisions, additions and assignments to Constitution or By-Laws being recommended.

The recommendations of the Board were referred back to the Committee on Constitution for a further rewriting of the proposed changes and the preparation of any other changes recommended in any part of the Constitution or By-Laws.

On motion by Dr. Lichty, seconded, and regularly carried, the following resolution was adopted:

RESOLVED: that the President shall send an explanatory note along with the final copy of proposed changes to the Constitution and By-Laws to each Fellow in order that members may more intelligently consider the prosposed changes and cast their vote accordingly.

It was recommended that the Committee on Credentials and the Board of Regents meet a day in advance of the Boston Clinical Session in order to complete outstanding business and the election of applicants.

Dr. George Morris Piersol, Chairman of the Committee on Credentials, presented the report of his Committee for disposal of applications for Fellowship, said report being unanimously adopted by the Board of Regents. (List of elections to Fellowship appears under "College News Notes" on another page).

The following resolution was adopted: RESOLVED, that the present existing ad-

vertising contracts in ANNALS OF INTERNAL MEDICINE be observed, but hereafter no advertisement of articles not approved by the Council on Chemistry and Pharmacy shall be accepted.

There was ageneral discussion concerning the eligibility of Anesthetists as a group for membership in The College. The Board ruled that Anesthetists are not considered eligible for membership in this organization.

General discussions concerning ritual, signing of the official roster, process of promotion of Associates to Fellows and other proposals for alteration of the Constitution and By-Laws were referred to the Committee on Constitution and By-Laws for further consideration.

Dr. Stewart R. Roberts (Fellow), Atlanta, Georgia, recently delivered a paper before the Third District Medical Society at Greenwood on "Nonvalvular Diseases of the Heart."

Dr. George B. Lawson (Fellow) was recently elected President of the Roanoke (Va.) Academy of Medicine for 1929.

Dr. James J. Waring (Fellow), Denver, was made President of the Colorado Society for Mental Hygiene at its recent organization.

Dr. Austin B. Jones (Fellow), Kansas City, spoke before the Clay County Medical Society at Excelsior Springs, October 25, on "Diagnosis and Treatment of Auricular Fibrillation."

Dr. Carl V. Vischer (Fellow,) Philadelphia, reported an interesting case of "Sarcomatosis," before the General Staff of the Hahnemann Hospital of Philadelphia on November 13th.

Dr. Daniel J. McCarthy (Fellow), Philadelphia, addressed the Philadelphia County Medical Society, November 28, on "Nervous Diseases in Conjunction with Visceral Disorders."

Dr. Charles F. Craig (Fellow), Lt. Col. M.C., U.S.A., addressed the Medical Officers of the District of Columbia recently on the Administrative and Professional Duties of Medical Officers.

Dr. Louis M. Warfield (Fellow), Milwaukee, addressed the Chicago Society of Internal Medicine at its one hundredth regular meeting on November 26, on "Hyperthyroidism."

"A Unified Plan of Tuberculosis Control" was the subject of Dr. Benjamin Goldberg (Fellow) before the annual meeting of the New York Tuberculosis and Public Health Association on November 2.

Col. Bailey K. Ashford, U. S. Army retired, represented the U. S. Army Medical Corps and the Government of Porto Rico as a delegate to the International Congress of Tropical Medicine and Hygiene at Cairo, Egypt, December 15-22.

Dr. Torald Sollmann (Fellow), Professor of Pharmacology and Materia Medica at Western Reserve University, Cleveland, Ohio, was appointed Dean of the School of Medicine of that institution by action of their trustees, following the resignation of Dr. C. A. Hamann on November 14th. Dr. Sollmann is an alumnus of Western Reserve University, and has been active on the faculty and various committees for several years. He is the author of many articles contributed to scientific journals and of text books. A recent text, of which Dr. Sollmann is joint author with Dr. Paul J. Hanzlik, is "An Introduction to Experimental Pharmacology," published by the W. B. Saunders Company. Dr. Sollmann is a member of the Council on Pharmacy and Chemistry of the American Medical Association, and a member of the Executive Committee of the United States Pharmacopeia.

The Pottenger Sanatorium, Monrovia, California, celebrated on December 5, 1928, the Twenty-fifth Anniversary of its opening. Ex-patients and many friends of the

institution attended a reception from eleven until two o'clock. At twelve o'clock, a buffet luncheon was served on the lawn, and in the evening, a dinner was given to former associates and assistants, members of the Trudeau Society and other local physicians. Dr. F. M. Pottenger, F.A.C.P., Medical Director of the Sanatorium, is to be congratulated upon the success of this institution.

Dr. Alfred Stengel (Fellow), and Dr. O. H. Perry Pepper (Fellow), both of Philadelphia, offered two postgraduate lectures on "Diseases of the Kidney" to a group of ninety physicians in Wilkes-Barre, Pa., during November.

At the Sixty-eighth Semi-annual Meeting of the Tennessee Medical Association at Columbia, November 22-23, Dr. Jack Withersoon (Fellow), Nashville, discussed "Remote Causes of Disability," Dr. J. O. Mainer (Fellow), Nashville, discussed "The Value of Rest and Exercise in the Treatment of Tuberculosis," and Dr. W. S. Leathers (Fellow), Nashville, discussed "Public Health."

Dr. Linn J. Boyd (Fellow), New York, is Editor-in-chief of the Journal of the American Institute of Homeopathy.

Dr. Carroll C. Pounders (Fellow), Oklahoma City, was guest of honor and delivered a talk on "Pediatrics," illustrated by lantern slides, before the Okmulgee-Okfuskee Medical Societies at Henryetta, Oklahoma, on November 12.

Dr. L. J. Moorman (Fellow), Oklahoma City, edits the section on Tuberculosis in the Journal of the Oklahoma State Medical Association. Dr. Moorman conducts the Moorman Sanatoria for the treatment of Tuberculosis, in Oklahoma City.

Dr. D. E. S. Coleman (Fellow), New York, is an Associate Editor of the Journal of the American Institute of Homeopathy.

Major articles have recently been contributed by Fellows of The College to The Journal of the American Medical Association as follows:

Dr. John A. Toomey, Cleveland
"Treatment of Scarlet Fever by Specific Antitoxins and Serums"

Dr. L. R. Sante, St. Louis
"Injuries to the Chest"

Dr. McKim Marriott (with Dr. A. F. Hartmann), St. Louis
"Newer Aspects of Acidosis"

Dr. R. S. Boles (with J. B. Carnett), Philadelphia
"Fallacies Concerning Chronic Appendicitis"

Dr. Cyrus C. Sturgis (with Dr. Millard Smith), Ann Arbor
"Pernicious Anemia"

Dr. W. W. Duke, Kansas City
"The Pollen Content of Still Air"

Dr. Harry M. Hall (Fellow), Wheeling, W. Va., is President of the West Virginia Medical Association. He and Dr. C. A. Ray (Fellow), Charleston, past President of the West Virginia Medical Association, delivered addresses, in connection with the School of Medicine program, at the inauguration of Dr. John Roscoe Turner as President of the University of West Virginia on November 28.

Dr. John William Shuman (Fellow) and Dr. Frederick Speik (Fellow), both of Los Angeles, addressed the Physicians and Surgeons of the South West at Albuquerque, November 9th, on "Lung Abscess" and "Associated Pathology of Gastric Ulcer," respectively.

Dr. Hans Lisser (Fellow), San Francisco, at Richmond, California, on October 13th spoke before the Contra Costa Medical Society on "Goiter Survey of the High Schools of Contra Costa County."

Dr. V. M. Longmire (Fellow), Temple, Texas, during October, addressed the Falls County Medical Society at Marlin on "Transfusions by the Citrate Method."

The November issue of the Journal of the American Institute of Homeopathy contained Articles by two members of The College as follows: "A Consideration of Renal Glycosuria" by Dr. E. Roland Snader, Jr., (Fellow) and "Clinical Aspect of Massive Collapse of the Lung" by Dr. Donald R. Ferguson (Fellow), both of Philadelphia.

Surgeon General E. R. Stitt (Fellow), U. S. Navy, was among the speakers at the Armistice dinner given by the Philadelphia County Medical Society on November 13.

Dr. Felix J. Underwood (Fellow), Jackson, Mississippi, was elected a Vice President of the Southern Medical Association at Asheville, November 14.

Dr. James G. Carr (Fellow) addressed the Annual All-Day Fall Clinical Meeting of the Adams County Medical Society at Quincy, Illinois, October 15, on "The Heart and the Electrocardiogram."

Dr. Harold Swanberg (Fellow), Quincy, Illinois, is Editor of The Radiological Review and the Chicago Medical Recorder. On the Editorial Board of this journal appear also the names of Dr. Leon T. LeWald (Fellow), New York; Dr. George E. Pfahler (Fellow), Philadelphia; Dr. Albert Soiland (Fellow), Los Angeles; and Dr. I. S. Trostler (Fellow), Chicago.

Dr. J. A. Bargen (Fellow), Rochester, Minnesota, spoke on "Etiology, Symptomatology and Medical Treatment of Chronic Ulcerative Colitis" before the Yorkville Medical Society on November 19.

Dr. E. Bosworth McCready (Fellow), Pittsburgh, delivered a lecture entitled, "Word-Blindness in School Children and its Influence upon Education, as a Cause of Retardation and as a Contributing Factor in the Diagnosis of Mental Deficiency" before the Department of Special Sub-Normal Class Teachers of the New Jersey State Teachers Association in Atlantic City on November 12.

Dr. Solomon Strouse (Fellow), Chicago, and Dr. Oliver P. Kimball (Fellow), Cleveland, addressed the Chicago Medical Society, November 7, on the "Treatment of Goiter" and "Science and Safety of the Prevention of Goiter," respectively.

Dr. Orlando H. Petty (Fellow), Philadelphia, addressed a Tuberculosis Conference at the Philadelphia County Medical Society on November 14, using as his subject, "Value of Health Examinations in Tuberculosis Prevention." Dr. Petty is Professor, Diseases of Metabolism, Graduate School of Medicine of the University of Pennsylvania.

Dr. Albert Soiland (Fellow), Los Angeles, addressed a special public meeting under the auspices of the Los Angeles County Medical Association, November 8, on "Cancer."

Maud Slye, Ph.D., who presented the results of her research at the New Orleans Clinical Session of The College, was another speaker.

Dr. Benjamin Hobson Frayser (Fellow), Ft. Harrison, Montana, was elected President of the United States Veterans Bureau Medical Society at its meeting at Helena, Montana, in early November.

Dr. Ralph Pemberton (Fellow), Philadelphia, delivered the twentieth Mary Scott Newbold lecture before the Philadelphia College of Physicians, November 7, on "Arthritis."

Dr. Pemberton also addressed the Northwestern Ohio District Medical Association at Lima recently on "The Control of Arthritis and Rheumatism."

Dr. John B. Youmans (Fellow), Nashville, and Dr. Stewart R. Roberts (Fellow), Atlanta, were speakers at the Second Councilor District Medical Society of Ohio at Dayton on September 24-28.

Dr. Lewellys F. Baker (Fellow), Baltimore, delivered the oration in medicine at the Havana Congress of the Pan American

Medical Association at Havana, December 29th to January 3rd.

Dr. O. H. Perry Pepper (Fellow), Philadelphia, presented a clinic before the Fayette County Medical Society of Pennsylvania at the Uniontown Hospital, November 15.

Dr. Wm. M. Sheppe (Fellow), Wheeling, October 9, presented a paper on "Bronchial Asthma" before the Lewis County Medical Society of West Virginia.

Dr. Herman N. Bundesen (Fellow), Chicago, was elected Coroner for Cook County on November 6. Dr. Bundesen was formerly Chicago's health commissioner.

Dr. Bailey K. Ashford (Fellow), Colonel, U. S. Army, retired, on November 16th spoke on "Sprue and the Relation of Its Anemia to Pernicious Anemia" before the University of Wisconsin Medical Society at Madison.

Dr. George Tryon Harding, Jr. (Fellow), Columbus, Ohio, is second in three generations of physicians in his family by the name of George T. Harding. His father, Dr. George T. Harding, Sr., was in practice up until about the middle of November, when he died suddenly while on a vacation.

Dr. George Tryon Harding, 3d, of Worthington, Ohio, is a son of Dr. George Tryon Harding, Jr. Warren G. Harding, late President of the United States, was a brother of Dr. George Tryon Harding, Jr.

Dr. John H. Musser (Fellow and President Elect), New Orleans, belongs to the six generations of physicians in the Musser family. Going back to the days of William Penn, we find that the first Musser to settle in this country received during the early part of the eighteenth century a "grant of land with the privilege of practicing medicine" in Lancaster County, Pennsylvania. Since that time, there have been six physicians in direct descent through the Musser family.

Dr. William S. Thayer (Fellow), Baltimore, was recently awarded the degree of doctor honoris causa of the University of Paris. Dr. Thayer is Professor Emeritus of Medicine at Johns Hopkins University, School of Medicine, and also an officer of the French Legion of Honor.

Dr. E. S. Lain (Fellow), Oklahoma City, addressed the Okmulgee-Okfuskee County Medical Society, October 8, on "External Markins of Drug Reactions."

Dr. Karl Rothschild (Associate), New Brunswick, N. J. read a paper on "Metal Poisoning with Presentation of a Case of Encephalopathy Following Lead Poisoning of Fourteen Years Duration" before the Staff of St. Peter's Hospital, New Brunswick.

Dr. Lea A. Riely (Fellow), Professor of Medicine at the University of Oklahoma School of Medicine; Dr. William Engelbach (Fellow), Professor of Medicine at the St. Louis University School of Medicine; Dr. Leonard G. Rowntree (Fellow), Professor of Medicine at the University of Minnesota Postgraduate School of Medicine and Chief, Section of Internal Medicine, Mayo Clinic; and Dr. William A. Jenkins (Fellow), Clinical Professor of Medicine at the University of Louisville School of Medicine, were on the faculty of the School of Medicine and University Extension Division of the University of Kansas for a series of intensive medical courses in Internal Medicine and Diagnosis given at Lawrence, Kansas, November 26-30, inclusive.

Dr. James Gray Carr (Fellow), Chicago, was recently made an honorary member of the Adams County (Illinois) Medical Society.

Dr. Harold Swanberg (Fellow), Quincy, gave an address on "Radium" before the Quincy Exchange Club on October 29th.

Dr. George Morris Piersol (Fellow), Philadelphia, is co-author with Dr. M. M.

Rothman, of an article entitled, "Liver Function Tests" in the December 8 issue of The Journal of the American Medical Association. In the same issue Dr. John P. Schneider (Fellow), Minneapolis, is co-author with Dr. James B. Carey of an article entitled, "Achlorhydria;" Dr. T. H. Coffen (Fellow), Portland, with Dr. H. P. Rush of an article entitled "Acute Indigestion in Relation to Coronary Thrombosis;" Dr. E. C. Trash (Fellow), Atlanta, with Dr. J. C. Massee of an article entitled, "Narcolepsy."

Dr. William W. Herrick (Fellow), New York City, addressed the Medical Society of the County of Queens, November 29th, on "Medical Complications of Pregnancy."

Dr. Herrick also delivered on December 7th before the New York Academy of Medicine an address entitled, "Certain Medical Complications of Pregnancy and Their Treatment."

Dr. Frederick G. Banting (Fellow), Toronto, on October 30th delivered at the University of Edinburgh the Cameron lecture, "giving an historical account of the researches that led to the discovery of insulin."

Dr. Howard T. Karsner (Fellow), Professor of Pathology at the Western Reserve University School of Medicine, addressed the Cleveland Academy of Medicine at its November meeting on "Abortus Infections and Clinical Medicine."

Dr. Robert S. Barghoff (Fellow) and Dr. Frederick Tice (Fellow), Chicago, were speakers at the meeting of the Illinois State Trudeau Society at Champaign on December 13th.

Dr. William F. Lorenz (Fellow), Madison, Professor of Neuro-psychiatry at the University of Wisconsin Medical School, recently addressed the Marathon County (Wisconsin) Medical Society on "Acute Encephalitis."

Dr. Robert M. Moore (Fellow), Indianapolis, spoke before the Indianapolis Medical Society, November 13th, on heart failure.

Dr. Andrew C. Ivy (Fellow), Professor of Physiology and Pharmacology at the Northwestern University Medical School, addressed the Milwaukee Academy of Medicine, October 19th, on newer physiology of the gallbladder.

Dr. Felix J. Underwood (Fellow), Jackson, Mississippi, was elected President of the medical alumni of the University of Tennessee recently. Dr. Underwood is State Health Officer for Mississippi.

Then and Now in Boston

Where We Meet, April 8-12, 1929

This article is furnished by the Boston Chamber of Commerce and is intended to give our subscribers interesting facts about our Convention City for 1929.

When you go to Boston, whether it is a matter of business or pleasure, you are going to enjoy yourself. The city has developed tremendously as a commercial and social centre within the last decade. Everywhere there is evidence of a wholesome spirit of enterprise and helpful co-operation in the fields of finance and manufacturing.

If on pleasure bent you will find that Boston possesses more "atmosphere" than any city on the eastern seaboard. Its historic buildings, famed the world over; the many unchanged pre-revolutionary scenes within easy motoring distance; its vista of rock bound coast and rose grown country lanes; a magnificent park system; beautiful suburbs quickly reached by railroad train and trolley car and its famed New England hospitality awaken a thrill of interest in the mind of the visitor.

Boston Town, you will remember, is nearly 300 years old. For it was in 1630 when the "Governor and Company of Massachusetts Bay in New England" sent out the first group of colonists headed by John Winthrop and because the principal men of the colony had lived in Boston, England, the name naturally was selected for their new home in America. And Boston has never lost its colonial flavor. The North End, Beacon Hill, Faneuil Hall, the Old State House, King's Chapel—a hundred reminders still linger, reminiscent of the days before Lexington called the thirteen original colonies to arms.

The reputation which Boston has long possessed of having narrow and tortuous streets is no longer true. In the downtown district, streets are crooked, but Boston has grown from "downtown," as from a common center and Newer Boston has beautiful thoroughfares, wide and straight. Commonwealth Avenue is one of the finest streets in the United States, with its beautiful homes and delightful parkway construction.

Parts of Boston are still old and full of flavor, much of which has not been swept away by the growth of population and of commerce. One still finds many a monument of historic interest that calls to mind Colonial Days, although large areas once inhabited by the choice names of Boston's social and literary history have been completely rebuilt or changed because of demolition and by the great fire of 1872.

Boston is situated at the head of Massachusetts Bay, and is the terminal for steamship lines connecting with all ports of the world. Its railroad and trolley lines connect the city with every other community throughout New England. The city is the trading centre for the 4,500,000 people who live within a fifty-mile zone.

Boston is the business, industrial and population centre of New England—the latter being one of the richest industrial regions in the world. The real Boston extends far beyond the Municipal boundaries.

Boston has one of the finest natural harbors on the Atlantic Coast, equipped with modern piers, docks and wharves. As a shipping point to commercial centres the city has a marked advantage over other

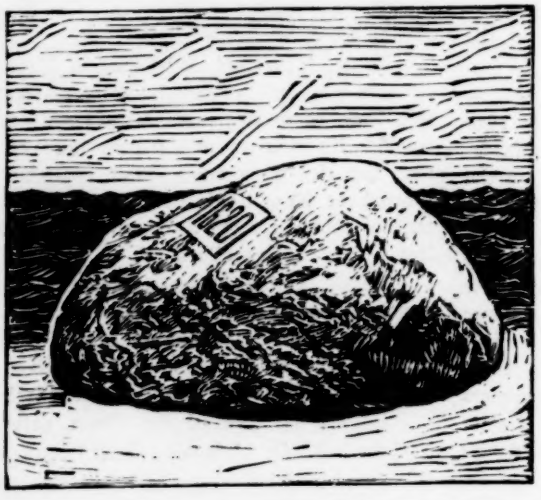
Main Gate at Harvard University—Oldest of American Educational Institutions. Established at Cambridge in 1636.

American seaports. It lies 200 miles nearer Europe than New York City; 1204 miles nearer Panama and the West Coast of South America than San Francisco; and 117 miles nearer Rio de Janeiro and Buenos Aires than Baltimore. As compared with any other American seaport, from 150 to 500 miles is saved by sailing from Boston to the ports of the United Kingdom, Continental Europe and the Near East.

Within easy distance of the city are many beaches; the Green and White mountain ranges with their magnificent scenery and grand views; woodlands and swift rivers, attractive in themselves, but especially appealing to hunters and fishermen; pleasure trips by steamer around Massachusetts Bay or up and down the coast of New England; or the real joys of out-of-door sports of a New England winter. The hard-surfaced highways bring all of these attractions within easy reach of the city proper.

Metropolitan Boston is the shoe and leather centre of the world; the headquarters of cotton manufacturing; it is the greatest wool market of the United States; is the most up-to-date fish port of the world, and in production is exceeded only by Grimsby, England; and is one of the three great rubber manufacturing centres of America. High quality confectionery is Boston's fifth greatest industry.

The steam and electric railroad mileage alone of Metropolitan Boston is greater than that of any similar area in the Western Hemisphere, and serves a population of 1,772,000 people.



Plymouth Rock, where the Pilgrim Farthers landed, "On a Stern and Rock-bound Coast," in 1620.

Boston is the natural radial point for the railroads of this section of the country and offers fast and frequent service to all parts of New England, to Canada, and West and South.

A unique example of cooperation between many municipalities which can scarcely be paralleled anywhere is offered in the Meropolitan Boston area. The Boston Metropolitan Park District comprises Boston and thirty-eight cities and towns within a radius of fifteen miles from

the State House, and consists of a chain of parks and boulevards which surprise the visitor by their extent and beauty.

The Metropolitan Water Department furnishes water to all the cities and towns within the Metropolitan District, and the system is a commendable engineering feat. Water is brought from the Berkshire Hills in Western Massachusetts to the Wachusett Reservoir in Clinton, forty miles from Boston, and from there brought into the Metropolitan area by a chain of smaller reservoirs—a complicated engineering effort.

House of Seven Gables — Salem. The original of Nathaniel Hawthorne's well known novel by that name.

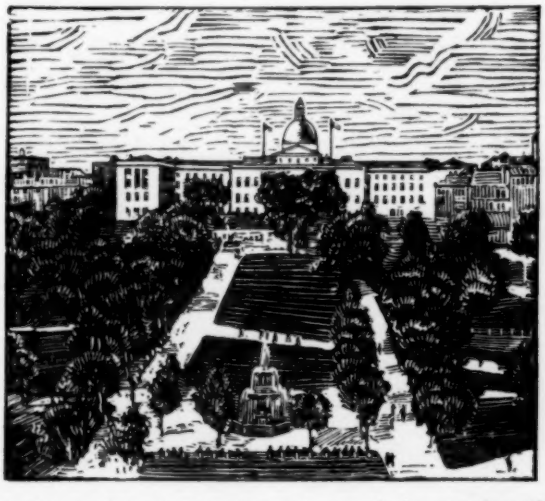
The development of aviation finds Boston equipped with an admirably located airport at Jeffries Point, less than two miles from the business centre of the city. Visiting pilots find there commercial hangar facilities. The landing field itself is unusually free from surrounding obstructions. It is used regularly by the Colonial Air Transport, which carries every day air mail from Boston to New York, the Boston Airport Corporation, the Regular Army, the National Guard and Reserve aviators.

A new airplane beacon light has been installed on the roof of a large department store as an aid to night flying.

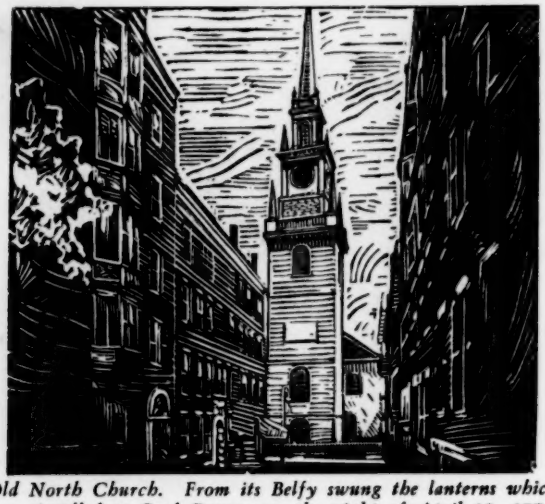
Boston is the first city in the world to inaugurate an all-day co-operative radio broadcast of news of interest to shoppers.

The theatres of Boston offer splendid opportunity to utilize their leisure time for entertainment and profit. Boston has ten "legitimate" theatres which bring to Boston the noted plays and the stage stars of the country. The city also has two-score moving picture houses, some of which are among the finest in the country.

Boston and New England are often called the "Birthplace of the American Nation," because of the historic richness of the region. In and around Boston are many places of attraction to every American who desires some time during his life to visit these historic shrines.



The Approach to the State House is one of the most beautiful scenes in Boston, viewed across the green expanse of Boston Common.



Old North Church. From its Belfy swung the lanterns which signalled to Paul Revere on the night of April 18. 1775.

Space will not allow the enumeration of a complete list of these. Yet there are certain of them that every visitor to the city ought to see.

A FEW OF THE HISTORIC PLACES IN BOSTON

BUNKER HILL MONUMENT — Monument Square, Charles town, commemorating the Battle of Bunker Hill, June 17, 1775. Winding stairway of 294 steps to top. Open 9 a. m. to 4 p. m. daily.

BOSTON COMMON — dates back to the beginning of Boston's history. It is situated in the heart of the city and is unique among Municipal public grounds. Its existence and preservation are due to the wise forethought of the first settlers. Four years after the settlement of the town it was laid out as "A place for a trayning field" and for "the feeding of cattell." A training field in part it has remained to the present day, and cattle did not cease to graze on it until the thirty's of the 19th Century. Every attempt to take away part of the land comprising the Common or the Boston Public Garden adjoining has met with determined resistance by the people of Boston.

KING'S CHAPEL AND BURYING GROUND—Tremont and School Streets. First chapel built in 1686, present one in 1749. Old English architecture. First Episcopal church in New England. Here British officers worshipped during siege. Became First Unitarian church in United States, 1785. Open daily 9 a. m. to 4 p. m.

Art Museum on Huntington Avenue—well worth a visit. Noteworthy on account of the Excellence of its Oriental Art objects.

OLD STATE HOUSE—Washington Street, head of State Street. Here the first Town House was built, 1657. Burned in 1711. The present building was built in 1713. Here met colonial courts and legislatures, the town and city governments and the General Court of the Commonwealth. John Hancock was here inaugurated first governor of Massachusetts in 1780. In front of it occured the Boston massacre. Here were the whipping post and the stocks. Open daily from 9 a. m. to 4 p. m.

OLD GRANARY BURYING GROUND — Tremont Street, between Beacon and Park. Here lie most of the personages of

historic Boston; seven early governors — Bellingham, Dummer, Hancock, Adams, Bowdoin, Eustis, Sumner; also Peter Faneuil, Paul Revere, the parents of Benjamin Franklin, the victims of the Boston Massacre; Robert Treat Paine, signer of the Declaration; John Phillips, first mayor of Boston; Elizabeth Goose ("Mother Goose") and many others. So called after 1737 from town granary on site of Park Street Church.

Concord Bridge, where was fired "The Shot Heard Round the World," in the memorable action, April 19, 1775.

"Old Ironsides"—(U. S. Frigate Constitution) launched at Boston in 1797, put into commission in 1798. Saw service in French War and War of 1812. One of the first frigates authorized under the Constitution of the United States, marking the beginning of the U. S. Navy as it exists today. Frigate at Boston Navy Yard, Charlestown.

Faneuil Hall—Merchants Row and Faneuil Hall Square. "Cradle of Liberty." Built in 1742 by Peter Faneuil and given to Boston as a town hall. Burned in 1761, rebuilt 1763. Focus of Revolutionary movement in Boston and the colonies. Enlarged 1805, from Charles Bulfinch's plans. Market below, public hall above, and armory of the Ancient and Honorable Artillery Company (chartered 1638) over all. Open 9 a. m. to 5 p. m. daily.

Boston Tea Party Tablet—Atlantic Avenue at Pearl Street. Boston Tea Party, December 16, 1773.

Boston Massacre—At head of State Street, corner of Exchange Street. March 5, 1770, the first bloodshed in the American Revolution.

Old North Church—Salem Street, foot of Hull Street, where on the evening of April 18, 1775, were hung the lanterns that gave warning of the British march on Concord and Lexington. Open 9 a. m. to 5 p. m. daily.

In or in Immediate Vicinity of Boston Are the Homes of: Paul Revere, Harrison Gray Otis and two Presidents, John Adams and John Quincy Adams.

Also Four American Poets :. Henry Wadsworth Longfellow, Ralph Waldo Emerson, James Russell Lowell and Oliver Wendell Holmes.

EDUCATION IN BOSTON

In New England were established the first free public schools mainained by taxation. The oldest American colleges are to be found in this region. Boston still is one of the first educational centres of the world.

In the Metropolitan Area are more than 200 unversities, colleges, normal and technical schools, music and art institutions and private schools.

Among them are Harvard University, Massachusetts Institute of Technology, Boston University, Tufts College, Wellesley College, Radcliffe College, Simmons College, Boston College, the New England Conservatory of Music and Boston Normal Art School. The first five — among the ten largest educational institutions in New England — have a total registration of over 20,000 students.

LIBRARIES

Metropolitan Boston contains 125 public libraries, with a total of nearly 3,000,000 books. Another 3,000,000 volumes are to be found in the colleges and special libraries.

Municipal Boston's world-renowned library at Copley Square with its thirty-one branches, has approximately 1,363,000 volumes and an annual circulation of about 3,400,000, more than two books apiece to every man, woman and child in its district. There is a library for each 24,000 of population.

MUSIC IN BOSTON

New England Conservatory of Music.
Boston Opera House.
Symphony Hall, the home of the Boston Symphony Orchestra.

ART IN BOSTON

Museum of Fine Arts.
Boston Public Library.
Fogg Museum of Art Harvard University.
Fenway Court. (The Isabelle Stewart Gardner Museum.)

SOME PLACES OF GREAT HISTORIC INTEREST NEAR BOSTON

Not only is Metropolitan Boston rich in historic shrines, but the same is true of all New England. Within short distances of the city and easily accessible is historic—PLYMOUTH, where the Pilgrim Forefathers settled in 1620.

SCITUATE, OF "OLD OAKEN BUCKET" FAME.

QUINCY, the birthplace of two presidents, John Adams and John Quincy Adams. Quincy also has the first incorporated railway in America, over which was hauled the granite for Bunker Hill Monument.

LEXINGTON, where the Minute Men defended American Liberty, April 19, 1775.

CONCORD, with its Sleepy Hollow Cemetery and the famous Bridge where was fired "the shot heard round the world," April 19, 1775.

SALEM, where is the "House of Seven Gables" and the Hawthorne home.

PROVINCETOWN, where stands the Pilgrim Memorial Monument, commemorating the first landing of the Pilgrim Fathers.

SUDBURY, in this community is the famous "Wayside Inn," scene of Longfellow's "Tales of a Wayside Inn," built in 1686, and now owned by Henry Ford.

CAMBRIDGE, the home of Harvard University, the oldest college in America; Longfellow's House; and the site of the Washington Elm, under which tree Washington took command of the American Army, July 3, 1775.

FITCHBURG TO NORTH ADAMS, Old Mohawk Trail, "the pathway trodden by the Indians of the Five Nations on their journeys from Hudson River to the Connecticutt."

FRANKLIN, N. H., birthplace of Daniel Webster.

HARTFORD, CONN., famed for "Charter Oak." Table on which President Lincoln signed the Emancipation Proclamation is in the Connecticutt State Library.